GENERAL LIBRARY
SEP 8 1913

BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL

Entered as Second-Class Matter at the Baltimore, Maryland, Postoffice.

Vol. XXIV.—No. 271.] BALTIMORE, SEPTEMBER, 1913. [Price, 25 Cents

CONTENTS.

	PAGE
Osteitis Deformans, Paget's Disease.—A Report of Six Cases Occurring in The Johns Hopkins Hospital and Dispensary. (Illustrated). By S. H. Hurwitz, M. D.	263
Diabetes in Early Infancy. By J. H. Mason Knox, Jr., M. D.	274
The Production of Passive Hypersensitiveness to Tuberculin.—Second Paper. By Charles R. Austrian, M. D., and Hiram Fried, M. D.	280
Some Striking Examples of Subnormal Accommodative Power. By Samuel Theobald, M. D.	282
Unilateral Sclerosis of the Pulmonary Artery. (Illustrated). By Frank A. Evans	284
The Value of Naso-Pharyngeal Surgery in the Treatment of Chronic Exudative Otitis Media. By H. O. Reik, M. D.	289
Notes on New Books	292

OSTEITIS DEFORMANS, PAGET'S DISEASE.*

A REPORT OF SIX CASES OCCURRING IN THE JOHNS HOPKINS HOSPITAL AND DISPENSARY.

By S. H. Hurwitz, M. D.,

Medical House Officer, The Johns Hopkins Hospital.

INTRODUCTION.

In the year 1876, Sir James Paget[1] presented before the Medical and Chirurgical Society of London a report on five cases of a "rare disease of bones." Six years later he was able to report seven additional cases to the same society[2] and by the year 1889,[3] he had seen 23 cases of this disease. Since his original communication, some 37 years ago, a large number of typical cases have been added to the literature; but osteitis deformans still remains a "rare disease of bones."

Higbee and Ellis[4] estimate that up to the year 1911 about 158 cases of osteitis deformans had been reported. This estimate is based upon the 66 cases collated from the literature by Packard, Steele, and Kirkbride.[5] During the 10 years following about 91 cases had been reported, 23 in this country and 68 cases abroad. In the two years, 1911 and 1912, I have found about 16 additional cases reported, of which approximately 10 are American. According to these figures about 175 cases of osteitis deformans are on record up to the present year.

It is of interest that the first case described in North America was that of MacPhedran,[6] of Toronto, in 1885, nine years after Paget's original communication. Watson,[7] of Baltimore, in 1898, and Elting,[8] of Albany, in 1901, reported the seventh and eighth of the American cases in The Johns Hopkins Hospital Bulletin.

The number of cases of osteitis deformans noted in America has greatly increased since 1901. According to Higbee and Ellis, the total number of American cases had reached 33 in the year 1911. These added to the 10 cases which I have been able to find in the literature and the six cases included in this paper would make a total of about 50 American cases up to 1913.

Osler has seen about three or four cases in private practice, and Dr. E. A. Locke of Boston has kindly permitted me to mention that during the past 12 years he has studied, and recorded notes on 40 cases of osteitis deformans, and that about 20 or 30 more have come under his observation.

The present report includes six cases; three of these have been found in the records of over 30,000 medical admissions to The Johns Hopkins Hospital, and three in the much larger number of admissions to The Johns Hopkins Hospital dispensary. Although all of the six cases present essentially the features of the disease described by Paget, the compara-

* Paper read before The Johns Hopkins Hospital Medical Society, May 5, 1913.

tive rarity of the affection has prompted me to put them on record. For the privilege of doing so I am indebted to Dr. L. F. Barker, in whose service these cases were studied.

CLINICAL RECORDS.

CASE I (Medical No. 30432).—On February 17, 1913, J. P., a tailor, white, aged 77, was admitted to the medical service of The Johns Hopkins Hospital, complaining of inability to use his right hand.

Family History.—The patient was not aware of any unhealthy inheritance; in fact, his father and mother had both lived to be nearly as old as the patient himself. With the exception of one sister, who has tuberculosis, all of his brothers and sisters are well. The patient feels quite sure that neither of his parents was ever subject to "rheumatism," and that none of the members of his family had a similar affliction. He has 11 children, eight sons and three daughters, all of whom are well, except one daughter, who has tuberculosis.

Personal History.—Before his thirty-fifth year, the patient had suffered from several exhausting infectious diseases; aside from whooping-cough, measles, and mumps, he had scarlet fever in childhood. During adolescence he suffered from repeated attacks of malaria, and at the age of 35 had cerebrospinal meningitis which impaired his hearing.

The patient is a tailor, and has practiced his trade for about 60 years without interruptions due to ill-health. Except for an occasional winter cough, and a little shortness of breath, he could boast of excellent health until he was about 50 years old, when he began to suffer from intermittent attacks of pain in the right shoulder, and later in the right hip. He remained active, however, and continued at his work. He boasts that at this period he was as straight as a "shingle," and in strength the equal of any other man of his age. Upon inquiry as to his height at this period, it was learned that he stood 5 feet 7½ to 8 inches. He says that at 60, his legs were so straight that he could hold a coin between his knees or between his ankles.

Present Illness.—The patient paid little attention to his occasional "rheumatic" pains and felt quite unaware of any changes in the shape of his body until 10 or 15 years ago, when the members of his family began to notice that he was beginning to stoop, and that his legs were becoming bowed. The patient was then 62 years of age. He, himself, soon began to notice that he was losing in height; for being a tailor by trade he noticed that the inner seam of his trousers was becoming shorter. This measurement had decreased from 33¾ inches to its present length of 30½ inches. From a height of 5 feet 7½ to 8 inches, he has fallen to a height of 5 feet 2 inches, a loss of 5½ to 6 inches in about 10 or 15 years. He has noticed also that his waist measurement has increased from 24 to 34 inches. As for the size of his hat, the patient does not furnish very definite information. He used to wear a No. 7¼ hat and now finds a No. 7⅜ a little small.

During the past few years, he has experienced a little awkwardness in the use of his legs: he finds some difficulty in separating them, and in placing one heel upon the opposite knee. In July, 1911, his ankles were swollen for a period of three weeks, and for the past few weeks he has had pain in his right hand. He has remained mentally clear and cheerful.

Physical Examination.—February 17, 1913. A general inspection of the patient immediately attracted the attention to the bony framework, which presented an unusual appearance. These alterations of the skeleton were most striking in the standing posture: a short, little man with a head which, though not in itself abnormally large, appeared definitely so when compared to the size of the body. The head is held slightly flexed over the chest; the latter is flattened in front, quite strikingly kyphotic in the upper dorsal region, and flares below. The pelvis is unusually broad and feminine in type. The crests are heavy and nearly in contact with the lower ribs, producing a diamond-shaped abdomen with a pendulous wall. The extremities show interesting features: the arms appear unusually long compared to the height. Both legs are bowed above and below the knees, which are widely separated.

The head itself does not present the changes which are often so striking in these cases. It is somewhat triangular in shape, with the base of the triangle uppermost. The sutures and fontanelles are tightly closed. The face appears small in comparison with the calvarium, and excepting the nose, the features are not prominent.

The shape of the thorax and its peculiar distortion can best be appreciated from the cyrtometer tracing. The tracing was made at the level of the fourth dorsal spine and shows how the anterior and posterior median lines are thrown out of alignment. The antero-posterior diameter is 3 cm. less than the lateral diameter, the greater portion of which, 14 cm., lies on the side with the more marked kyphosis. Anteriorly, the thorax is flattened above, but the angle of Ludwig is prominent. The costal angle measures about 135 degrees.

The right clavicle presents a most unusual appearance. It is much thickened and roughened, although not nodular. There is an extreme accentuation of the normal curves. The ribs are also somewhat thickened and broadened and somewhat ankylosed to the articulating processes of the spine, thus greatly limiting the free movements of the thorax.

Upper Extremities.—The radius and ulna of each forearm is definitely bowed. This bowing is more marked on the left than on the right. No definite roughening or thickening of these bones can be made out.

The striking feature is bowing of both legs. The femora feel thickened and are bowed outward. The tibiæ also are broader and thicker, but not roughened or nodular; the latter show both anterior and lateral bowing. The knees are slightly more prominent than normal. Both patellæ are thickened, the left more than the right; the circumference of the left knee through the midpatellar region measures 36 cm., and that of the right 34 cm. With the patient lying flat in bed and the heels together, the distance between the two medial condyles is 11 cm. The difference between the measured length and the apparent length of the legs is 7 cm. on the right and 6.5 cm. on the left, due to the bowing and the shortening in Bryant's line. The shortening of Bryant's line points to a change in the angle between the neck and shaft of the femur, producing a coxa vara. This is well shown in the skiagram of the hip joint.

MENSURATION OF PATIENT.

HEAD.

	cm.
Occipitofrontal circumference (maximum)	60.5
Occipitofrontal diameter	20.5
Occipitomental diameter	20.0
Biparietal diameter	17.0
Suboccipito-bregmatic diameter	18.0
Suboccipito-bregmatic circumference	55.5
Bitemporal diameter	13.0
Circumference of vault, from meatus to meatus	37.0

THORAX.

Antero-posterior diameter (tracing)	23.0
Lateral diameter	26.0

PELVIS.

Intercristal diameter	32.5
Interspinous diameter	30.0
Intertrochanteric diameter	32.0

UPPER EXTREMITY.	Right. cm.	Left. cm.
Length of arms (tip of acromion to styloid of radius)	54.0	54.0
Length of upper arm (tip of acromion to ext. condyle humerus)	30.5	30.0
Length of forearm (ext. condyle to styloid of radius)	27.0	27.0
Grand expansion of arms (66.2 inches), 165.5 cm.		
LOWER EXTREMITY.		
Antero-superior spine to internal malleolus	83.5	84.0
Bryant's line	5.5	5.5
Great trochanter to ext. condyle of femur	41.0	42.0
Ext. condyle of femur to ext. malleolus	44.0	43.0
Circumference of knee (mid-patellar region)	34.0	36.0

Height.—5 feet 2 inches. Height before onset of disease about 5 feet 7½ to 8 inches, a loss of 5½ to 6 inches. Calculated from the grand expansion of the arms the loss in height would be at least 4 inches.

General Examination.—Numerous lipomata over trunk and upper and lower extremities. No general glandular enlargement. Thyroid is not felt. *Lungs* show slight signs of emphysema. The conjunctival tuberculin test is negative. *Cardio-respiratory system:* cardiac dullness is not enlarged. Aortic second is ringing in quality. There is marked sclerosis of all the peripheral vessels, temporals, brachials, and radials. The blood pressure averages 140 (Tycos).

Examination of the fresh blood and of stained smears showed no abnormalities. The Wassermann reaction was negative.

Examination of the urine and fæces showed no abnormalities.

An ophthalmological examination showed a slight clouding of the lens in the left eye; both discs were well outlined; the arteries thin and tortuous; no hemorrhages or exudate on either fundus.

Radiographical Examination (Skiagram No. 17014. Reported by Dr. F. H. Baetjer).—*Skull* shows a uniform deposit of new bone, making the total thickness nearly one inch. Sella very irregularly shaped, but present. *Right tibia* shows no increased calcification, but a marked osteoporotic condition. *Left tibia* shows increased calcification especially on the anterior surface. There is also some osteoporosis confined largely to bone around medullary cavity. Both tibiæ show well marked bowing. *Fibulæ* both show longitudinal osteoporosis. *Pelvis:* heads of both femora are slightly bent, producing coxa vara; marked osteoporosis of necks and great trochanter; both illi show osteoporosis in the bodies. Both pelvic bones show increased calcification, but no osteoporosis. Both femora are bowed. *Hand:* first phalanges all show marked porosis. The middle phalanges of index and fifth fingers show same condition; whereas those of third and fourth fingers show distinctly increased calcification. The third and fourth metacarpals are shorter than normal.

Summary of Case I. The chief features of this case are: First, the insidious onset of the disease at the age of 50 with vague rheumatic pains and its gradual progress until the age of 62, when the stooping of the body and the bowing of the legs had become well marked; thus the pains antedated the actual bony changes by about 10 years; second, the only slight discomfort to the patient produced by the gradually progressing deformity; third, the presence on examination, of the characteristic posture, the large calvarium, the bowing of the femora, tibiæ, radius, ulna and the dorsal kyphosis and prominent right clavicle; fourth, the loss of 5½ to 6 inches in height; and fifth, the presence in the skiagrams of the typical bony changes of the disease.

CASE II (Disp. No. E. 81938).—J. B., a white male, aged 74 years, first came to the Johns Hopkins Hospital dispensary about 10 years ago complaining of swelling of the legs. When seen again on March 16, 1913, the patient compiained of " misery in the stomach, and shortness of breath."

Family History.—There is a suspicious tuberculous history among the immediate members of the family. The father died at the age of 42 of a "cold"; the mother died at about the same age of "congestion of the throat"; three brothers are all dead, one died at the age of 60, of pneumonia; one was crippled all of his life by a "white swelling of the hips and back"; and a third brother died at 24. Of two sisters who are dead, one died during childbirth, and the other of a "cold." The patient does not know of any heart disease, kidney disease, cancer or rheumatism in the family. He is not aware that any one in the family suffered from a deformity similar to his; except that his paternal grandmother became stooped between the ages of 50 and 60.

Past History.—The patient does not recall any diseases of childhood. In 1869, 44 years ago, he had typhoid fever and was ill for six weeks. He has always had a poor appetite, which has become worse during the past few years. He has been troubled with hemorrhoids for about 40 years.

In October, 1909, the patient returned to The Johns Hopkins Hospital dispensary complaining of constipation, headaches, and poor appetite. He states that he began to have a feeling of fullness and distention after eating, which has persisted up to the present time.

For about 10 years, the patient has suffered from swelling of the ankles; up to about five years ago, this œdema was transient, but has been more constant since then. He has suffered from catarrh for about 40 years, and complains occasionally of a cough. For the past few years, he has become very short of breath. He has had nycturia for about 30 years and now complains of increased frequency of micturition.

Present Illness.—The patient has paid little attention to his gradually progressing deformity. In fact, during the last few years, he has attended the dispensary at irregular intervals but has not complained of the bowing of his legs, which according to the history notes, has been becoming more prominent.

Upon questioning the patient further, the latter states that about 20 years ago, when he was about 54 years old, his friends would tell him to straighten up, because he was getting "full-breasted" in the back. He thinks that his height at this period was about 5 feet 7 inches. He, himself, never noticed that his legs were becoming bowed, but he was told so by the doctor at this dispensary about 10 years ago. He has not paid any attention to changes in the size of his head, but thinks that he wears a larger hat now than formerly. During the past year the size of his hat has increased from No. 6⅞ to No. 7.

Physical Examination.—March 16, 1913. The patient is a short, stooped, emaciated old man of 74 years. His supraorbital ridges are prominent and his eyes appear sunken in their orbits. There is a well marked arcus senilis; the pupils react to light and on accommodation. The temporal arteries are visible and tortuous. Mucous membranes are somewhat pale. Tongue is furred. There are no teeth in either jaw.

The patient's head looks top-heavy. The calvarium is squarish in shape, and bulges in the frontal, occipital and parietal regions. Over these areas, as well as over the vertex, there can be felt a few rounded, nodular elevations. With the exception of the nose, the features are small in comparison with the size of the calvarium.

In the natural standing posture, he presents an unusual appearance. Viewed laterally, the deformity of the body resembles the shape of the letter S, the dorsal kyphosis contrasting markedly with the bending and forward bowing of the legs. The head is held forward, and downward, and the arms appear unusually long for the height.

The chest looks as if it had sunken into the pelvis, the costal margins and crests of the ilia being nearly in juxtaposition. The antero-posterior diameter of the thorax is slightly greater than

the lateral diameter. (The greatest kyphosis is at the level of the 6th dorsal spine.) The clavicles are not unusually prominent, but the supraclavicular fossæ are deep. The angle of Ludwig is prominent, and the costal angle narrow. The ribs are closely approximated and feel slightly thickened. The spine is rigid and immobile.

The abdomen is diamond-shaped. Just below the costal margins there is a well marked transverse furrow, below which the abdomen is pendulous. The bony pelvis flares out and is broad and capacious. The iliac crests are thickened, measuring 3.5 cm. in width behind the antero-superior spines, and feel rough. The external lips overhang the iliac bones.

Lower Extremities.—The lower extremities are in a position of genu varum. With heels together the knees are separated 12 cm. from one another, as measured between the two internal condyles of the femora. Both femora are bowed outwards and slightly anteriorly, the left more than the right. The bones feel a little thickened and roughened. Due to the extensive œdema of the legs, the lateral bowing of the tibiæ is not apparent, but the anterior bowing is very pronounced. There is also some irregularity and thickening of both tibiæ. Feet are not involved.

Upper Extremities.—Both humeri feel thickened in the upper third, but no definite bowing can be made out. The radius and ulna on each side are definitely bowed, the left more than the right. The surfaces of these bones are not thickened or roughened. Fingers are small and narrow. Soft parts not increased.

MENSURATION OF PATIENT.

HEAD.

	cm.
Occipitofrontal circumference (maximum)	58.0
Occipitofrontal diameter	17.5
Occipitomental diameter	23.0
Biparietal diameter	15.0
Suboccipito-bregmatic diameter	17.0
Suboccipito-bregmatic circumference	55.0
Bitemporal diameter	13.5
Circumference of vault, from meatus to meatus	36.0

THORAX.

Circumference: sixth dorsal spine	81.0
Antero-posterior diameter (tracing)	26.0
Lateral diameter (tracing)	25.0

PELVIS.

Intercristal diameter	31.0
Interspinous diameter	28.0
Intertrochanteric diameter	31.5

UPPER EXTREMITY.	Right. cm.	Left. cm.
Length of arms (tip of acromion to styloid of radius)	56.5	54.5
Length of upper arm (tip of acromion to ext. condyle of humerus)	33.0	32.0
Length of forearm (ext. condyle to styloid of radius)	26.0	25.0

Grand expansion of arms (66 inches), 167 cm.

LOWER EXTREMITY.

Antero-superior spine to internal malleolus	81.5	80.0
Bryant's line	6.0	5.5
Great trochanter to ext. condyle	44.5	42.0
Ext. condyle to ext. malleolus	40.5	39.5
Circumference of leg (mid-patellar region)	35.0	37.0
Circumference of leg (15 cm. below patellar region)	34.5	35.0
Circumference of leg (ankle)	23.0	25.0

Height.—4 feet 11¾ inches. Height before onset of disease, 5 feet 7 inches, showing a loss of 7¼ inches. Recorded height in April, 1910, is 5 feet 1¾ inches, showing a loss in two years of 2 inches. Calculated from the grand expansion of the arms, the loss in height is estimated at 6¼ inches.

Visceral Examination.—Lungs: thorax expands as a whole, the upper left front a little more than the right. Vocal fremitus is well transmitted over both lungs in front; the percussion note is hyperresonant; slight impairment at apices. Breath sounds are emphysematous in type and inspiration is accompanied by a few fine crackles. Tuberculin conjunctival test, both 1 per cent and 5 per cent negative.

Cardiovascular.—Visible pulsation in fifth intercostal space. No shock or thrill. Cardiac dullness begins over third rib and extends 11 cm. to the left and 5 cm. to the right over the fourth rib. At the apex the first sound is followed by a short systolic murmur, transmitted to the axilla. Sounds at base are clear and of equal intensity. Pulse is regular, small volume. Radials and brachials are beaded and hardened. Blood pressure 180 (Tycos).

Urine shows a trace of albumin.

Abdomen.—Breathing is chiefly abdominal due to, more or less, ankylosis of ribs. The abdominal walls are soft. There is slight tenderness in the epigastrium on deep palpation. Liver dullness reaches just to costal margin. Spleen and kidneys are not palpable.

Genitalia.—There is enlargement of both external inguinal rings with definite impulse on coughing.

Reflexes.—Present in both upper and lower extremities.

Radiographical Examination (Skiagram No. 17297. Reported by Dr. F. H. Baetjer).—*Skull:* sella normally shaped; of solid type. Bones show uniform thickening; thickening is symmetrical and not so irregular as in Case I. Thickness one-half inch.

Tibia and Fibula (left).—Tibia markedly bowed anteriorly, and irregularly thickened with longitudinal areas of porosis. Fibula shows very little increased calcification, but on the contrary, large areas of longitudinal porosis. The right tibia shows the same condition, but to a less degree.

Summary of Case II.—Certain points in the history of this case are deserving of special mention: First, the slow painless progress of the disease. The disease began at the age of 54, but the patient did not complain of any symptoms until 10 years later; then he sought medical aid, not for his deformity about which he was practically unaware, but for the symptoms of myocardial insufficiency, due to the embarrassment of the circulation by a deformed thorax; second, the case illustrates, in an unusual way the typical changes in the skeleton wrought by osteitis deformans: large square head, marked kyphosis, bowing of both femora and tibiæ; third, the loss of 7¼ inches in height; fourth, the skiagrams of the case show excellently the changes in the long bones, the porosis and calcification so characteristic of this disease.

CASE III (Disp. No. E. 86138).—R. W., white, aged 53, came to the orthopedic division of The Johns Hopkins Hospital dispensary in 1912, complaining of pain in "both hips, right knee, and right shoulder."

Family History.—The patient's family history is of interest since there is some evidence that the mother of the patient was similarly afflicted. His mother lived to the age of 87 years. Up to the age of 50 or 60 her health was good. At this time she began to complain of "rheumatism." These rheumatic pains were associated with swelling and bowing of the legs. According to the account of the patient's wife, "mother and son were the image of one another." Aside from the patient's mother, no other members of the family had any similar trouble. The patient's father died at the age of 62 years of a "chronic cough." One brother and one sister died in middle life. There is no history of heart disease, nephritis, or malignant disease in the family.

Past History.—The patient can boast of good health until the onset of the present illness. He cannot recall any diseases of childhood. His birth was normal and his development uneventful. He is quite sure that he was a well nourished baby without any of the stigmata of rickets. There is no history of any infectious diseases during adolescence and manhood. He has had periods of shortness of breath and palpitation. Denies gonorrhœal and luetic infections. The patient has three healthy children and his wife has never had any miscarriages.

About 15 years ago, the patient received an injury to his right ankle which disabled him for six weeks. After recovering, he did not notice any difference in the usefulness of his right leg.

Present Illness.—It is difficult for the patient to state definitely when the changes in his body began. About 10 years ago, when the patient was 42 years old, he began to suffer pain in his right hip, and right leg. Both of his legs became swollen and the patient's wife noticed that his right leg was beginning to bend. Later the left leg became bowed. A few years after the onset of his illness, the patient came to this dispensary for treatment and after a long absence, returned in February, 1912. The pains in his hips have continued to the present time. Now, he complains also of cramp-like pains in the calves of his legs, which keep him awake at night. Both his right knee and right shoulder have become painful. For the past five years he has had transient œdema of the ankles and feet; this is gradually becoming more constant.

For the past 10 years his friends have noticed that he was becoming stooped and deformed. From a height of 5 feet 7 inches, at the age of 38, he has fallen to his present height of 5 feet 3⅛ inches, a loss of 4 inches. The right leg, where the bowing started, has progressed more than the left in this process, so that it is now considerably shorter than the left. To equalize this difference in length of the two legs, the patient must wear a higher heel on the right shoe. During the past six years the patient himself has noticed that he was buying larger hats. A cap worn by the patient six years ago measures 6⅞, whereas the patient now wears a No. 7¼.

The patient is a driver of a delivery wagon. In spite of his affliction, he still finds it possible to continue his work. He does, however, feel more clumsy and awkward than formerly in the use of his legs, especially in getting on and off the wagon.

His general health has remained good, and although he has become depressed on account of his condition, there is not the slightest evidence of any mental deterioration.

Physical Examination.—March 9, 1913. The patient is an undernourished man of 54. His stunted appearance, heavy head, and bowed, waddling legs immediately attract the observer's attention. Aside from a little looseness of the skin, a slight pallor and some pyorrhœa and dental caries, there is little of importance in the general survey.

The attitude of the patient, while standing, is almost pathognomonic of the disease: the body is small and stooped, the legs are markedly bowed, laterally and considerably anteriorly. The head appears out of all proportion to the size of the body. One gets the impression that the weight of the head has produced an anterior bowing of the cervical spine. This enlargement of the head is entirely of the calvarium, especially in the parietal and occipital regions. The features are not accentuated; the lower jaw does not protrude.

The thorax shows a well marked kyphoscoliosis in the middorsal region, the convexity of the scoliosis being slightly more to the left. The right clavicle is more prominent than the left, though this difference is not striking. There is considerable flaring of the thorax below, producing a wide costal angle (about 120°).

The abdomen is slightly prominent and there is no well defined furrow separating it from the thorax above. It is definitely wider laterally than is normal. So that the distance from ensiform to symphysis pubis about equals the lateral diameter between the two anterior superior spines. The pelvis is feminine in type, being broader, flatter, and thicker than usual. The iliac crests are broad and thick; the external lip is accentuated and overhangs the bones.

Lower Extremities.—Both legs are markedly bowed, due to the outward bowing of both femora and tibiæ; this bowing is more marked on the right. There is well developed anterior bowing of both tibiæ. The right leg is definitely shorter than the left, the internal malleolus on the right side being 4 cm. higher than on the left. The knees are in a position of genu varum. With the heels together, the knees are separated a distance of 9 cm. as measured between the two internal condyles. Both patellæ are slightly thicker than normal.

The tibiæ feel thick, coarse, and nodular. Well marked œdema of the ankles is present on both sides. No œdema is present on the dorsum of the feet. The toes appear normal and the feet show no changes.

Upper Extremities.—The arms, except for their appearance of disproportionate length, are apparently only slightly affected. Both humeri feel a little roughened in the upper third. There is no change in the radius and ulna of the right arm. The radius on the left is slightly bowed. Hands are small and pudgy. Fingers short and thick. No signs of bony deformity or thickening.

MENSURATION OF PATIENT.

HEAD.

	cm.
Occipitofrontal circumference (maximum)	59.0
Occipitofrontal diameter	20.0
Occipitomental diameter	22.0
Biparietal diameter	15.5
Suboccipito-bregmatic diameter	19.5
Suboccipito-bregmatic circumference	54.5
Bitemporal diameter	12.0
Circumference of vault from meatus to meatus	38.0

THORAX.

Circumference (sixth dorsal spine)	83.6
Antero-posterior diameter (cyrtometer tracing)	23.0
Lateral diameter	30.0

PELVIS.

Intercristal diameter	29.0
Interspinous diameter	25.5
Intertrochanteric diameter	32.0

UPPER EXTREMITY.	Right. cm.	Left. cm.
Length of arms (tip of acromion to styloid of radius)	56.0	54.5
Length of upper arm (tip of acromion to ext. condyle of humerus)	30.5	32.5
Length of forearm (ext. of condyle of humerus to styloid of radius)	25.5	20.5

Grand expansion of arms (68 inches), 173.5 cm.

LOWER EXTREMITY.

Antero-superior spine to internal malleolus	82.5	84.5
Bryant's line	4.0	5.5
Great trochanter to external condyle	40.0	40.5
External condyle to external malleolus	41.5	40.5

Height.—Present height is 5 feet 3⅛ inches. Height before onset of disease 5 feet 7¼ inches, which corresponds approximately to the measurement of the grand expansion of the arms, showing a loss of about 4 inches in height.

Visceral Examination.—Lungs: thorax expands only slightly on deep inspiration. Breathing is chiefly diaphragmatic. Percus-

sion note is hyperresonant; breath sounds are emphysematous in type. *Heart and Vessels:* apex beat can be well localized in fifth intercostal space, in the mammillary line. Cardiac dullness begins over the third costal cartilage and extends 11 cm. lateral to mid-sternal line in fifth intercostal space and 4 cm. to the right over the fourth rib. Cardiac action is irregular. At the apex the first sound is followed by a faint systolic bruit, not well transmitted. At the base both sounds are clear. Pulse is of large volume, very irregular in force and rhythm. Temporals, radials, and brachials are tortuous and sclerosed.

Blood pressure 125 (Tycos).

Abdomen.—The abdominal walls are soft. No generalized or localized tenderness. Liver dullness ends at costal margin. Liver and spleen are not felt.

Reflexes.—Present in both upper and lower extremities. Normal plantar response.

Radiographical Examination (Skiagram No. 12562. Reported by Dr. F. H. Baetjer).—*Skull* shows thickening of inner and outer tables with flocculent deposits of bone, irregularly placed over the entire outer table. Sella turcica is slightly enlarged and of solid type. *Tibia* shows marked thickening, especially of the anterior surface with small areas of porosis. *Femur* shows the same condition.

Summary of Case III.—It is of interest that in this patient the disease began in the fifth, rather than in the sixth decade, as in the two previous cases. The symptoms of onset, as in Case I, were vague rheumatic pains in the right hip and right leg, the latter being the first involved in the bowing. The skeletal parts show the usual changes with a marked increase in the circumference of the head and the loss of about four inches in height. The history of trauma to the right ankle, five years before the onset of the first symptoms, calls for the mention of injury as an etiological or predisposing cause. Several of the recorded cases, including Paget's original case, and that of Packard, Steele, and Kirkbride, gave a history of trauma.

If the patient's account be correct, and if one can rely on photographs, the mother of the patient began to develop the disease at the age of 60. This is of interest in connection with the view that heredity is an important factor in the etiology of this affliction.

Case IV* (Medical No. 13120).—O.W. S., white, a carpenter, 59 years old, was admitted to the medical service of The Johns Hopkins Hospital on July 10, 1901, complaining of dropsy, dimness of vision, and stomach trouble.

Family History.—The patient's father died of old age, and his mother died of heart disease. For years before her death, the patient's mother suffered from rheumatism. There is no history of gout, cancer, or tuberculosis among the members of the family.

Past History.—The patient cannot recall any diseases of childhood. Excepting small-pox in the year 1859, no mention is made in the history of any illness until 25 years ago, when the patient had a sun-stroke. At this time, he was ill for several months and thinks that his whole system suffered considerably from the shock. For about 15 or 20 years he had suffered from dyspepsia and attacks of diarrhœa, and was very susceptible to any indiscretion in diet. During the past few years, he has complained of a weak back and irregular attacks of "rheumatism," which, however, have not incapacitated the patient from his usual work.

The changes in the shape of his body had scarcely attracted his attention, although he had noticed that his hat was one-half inch larger in size, and that the bones of his legs were thicker, and his back more bowed. At the time of admission, he was three inches shorter than formerly.

Habits.—The patient has been a hard worker at his trade. He does not use alcohol, but has smoked and chewed all of his life.

Present Illness.—One year before admission, when the patient was 58 years of age, he began to have lassitude, weakness, shortness of breath on exertion, and quite general œdema. Three months ago he had his first syncopal attack: sudden loss of consciousness and dimness of vision, lasting for 20 minutes, followed by diplopia, tinnitus and giddiness. Nycturia and polyuria now became troublesome symptoms: the patient has had to void about every two hours, and has noticed that the color of his urine is darker.

For the past two months he has had diarrhœa, and has lost about 35 pounds in weight. More recently he had been troubled by stiffness in the muscles of his neck, and pain in the back of his head and over the left eye.

Physical Examination.—The patient is a sparely nourished man. The striking features on examination are the osseous changes: the head is unusually large for the size of the body, the enlargement being most striking in the occipital and parietal regions. The circumference of the head about the brow measures 59 cm.; the antero-posterior diameter is 21 cm., the lateral diameter 17 cm. With the exception of the bridge of the nose, which is unusually broad, the bones of the face show no changes.

Thorax.—The neck is short and the head is closely set on the thorax. There is a marked pigeon breast and a high grade of dorsal bowing of the spine. The most marked kyphosis is in the upper dorsal region, so that the antero-posterior diameter at this point is increased, being 25 cm. as compared to a lateral diameter of 21 cm. The thorax, which is narrow above, flares markedly at the costal margin. Both clavicles are unusually prominent and bowed.

The *abdomen* is much foreshortened in the vertical diameter, the space between the costal margins and iliac crests being about a finger's breadth. There is a transverse furrow below the margin of the ribs.

Extremities.—There is marked atrophy of the muscles about the shoulder girdle, and considerable muscular weakening of the upper and lower extremities. The patient is unable to completely extend the forearm on the arms. Both humeri are practically normal. There is a definite bowing of the ulna and the radius on both sides. No epiphyseal thickening can be made out.

Both femora are markedly bowed outward. Both tibiæ show distinct bowing outward and forward. There are no localized nodular thickenings along the course of the long bones and no areas of tenderness.

The patellar reflexes are active on both sides.

The general examination showed only marked arteriosclerosis, slight cardiac enlargement, and a little bronchitis and emphysema. There was little evidence of heart disease. In the urine, there was a trace of albumin, but no casts.

Examination of the eye grounds showed no abnormalities in the fundi.

Summary of Case IV.—In this case, as in Case II, the symptoms which brought the patient to the hospital were dependent upon arteriosclerosis and myocardial degeneration, and had no direct relation to the disease. The onset had evidently been so insidious and the evolution of the disease so slow and gradual that the patient had little knowledge of the changes in his bony framework. For this reason, it is difficult in this case to determine the exact age of onset, though Emerson, in referring to this case, placed it at 58.

Case V (Medical No. 20609).—T. P. H., white, a potter, aged 67, was admitted to The Johns Hopkins Hospital on January 7, 1907, complaining of "asthma."

Family History.—The father of the patient died of sun-stroke at the age of 66 years. The patient's mother died of pneumonia at 62 years. One brother died when young. Two sisters of the

* Both Cases IV and V are mentioned by Emerson in his article on Paget's Disease in Osler's Modern Medicine, 1909, VI, 717.

patient are alive and well. The patient feels certain that no other members of his family have had any deformities similar to his. Both his father and grandfather were erect until the day of their deaths. The patient's father suffered from rheumatism.

Past History.—The patient has always been a strong, and fairly well man. He had rheumatism when 16 years of age, but has had no attacks until his recovery from "chills and fever" 16 years ago, when the patient was 51 years old, since which time he has had "rheumatism" in various joints. Of late, he has had headaches. His vision has been failing for the past year, and about one and one-half years ago he began to be deaf. The "asthma," of which he complains, came on insidiously and comes and goes. He has had no gastro-intestinal disturbances until five or six years ago, when he began to have poor control over his anal sphincter. Of late he has lost entire control of his bladder and rectum.

Present Illness.—For the past year the patient has been unable to work. The asthmatic attacks, which began insidiously, have grown gradually worse. He has a tight feeling in the chest with very little sputum and no pain on coughing.

The patient apparently knows very little of his deformity. Upon closer questioning it was learned that the first change in his stature began after his attack of "malaria," 16 years ago, when the patient was 51 years old. The beginning of these changes was associated with "rheumatism." It was about this time that the patient's sister noticed the change in her brother's height.

Physical Examination.—The bones of the cranium are greatly enlarged, the enlargement involving especially the frontal, temporal, parietal, and occipital bones. The bones feel normal and present no fossæ. There is no enlargement of the bones of the face, which is small in comparison to the calvarium. The eyes are small and appear tucked under a large brow.

The following are the measurements of the head:

	cm.
Bitemporal diameter	14.00
Biparietal diameter	18.00
Occipitofrontal diameter	19.25
Circumference in O. F. diameter	60.00
Occipitomental diameter	19.75
Suboccipito-bregmatic diameter	19.00
Circumference in S. O. B. diameter	50.00

Thorax is greatly deformed and asymmetrical. A marked kyphosis and scoliosis, mainly in the mid-dorsal region constitutes the essential deformity. The convexity of the scoliosis is to the right, producing a bulging of the thorax on the right side, and a corresponding flattening on the left side. The flaring at the costal margins produces a wide epigastric angle. The clavicles are prominent. The circumference of the thorax at the top of the axilla measures 85 cm. of which the right side measures 44 cm. The antero-posterior diameter measures 28.1 cm., whereas the lateral diameter measures 26.1 cm.

There is some bowing of the radius, ulna, and humerus, with the concavity backwards. This bowing is much more marked in the left radius. The long bones of the lower extremities are markedly deformed. Both femora are bowed and the tibiæ have an outward and anterior curve. Both ankles are œdematous.

The estimated height of the patient at the age of 27 is 5 feet 8 inches as compared to a height of 4 feet 6¼ inches on admission, showing a loss of 13¾ inches in stature.

Examination of the lungs and cardio-vascular system showed little more than signs of emphysema, chronic bronchitis, and advanced arteriosclerosis. A systolic murmur heard at the apex is transmitted to the axilla. The urine showed no albumin or casts. The blood pressure averaged 145 mm.

The ophthalmological examination showed a streak of opacity in the right cornea and cataracts in both eyes.

On examination, the blood showed a slight anæmia and a differential count of stained smears showed a fairly normal percentage of the different cellular elements.

Summary of Case V.—This case belongs with Cases I and III, to the painful group. The disease began at the age of 51 with "rheumatic" pains in various joints and bowing of the legs. The loss of height in this case is far greater than in any of the other four cases; it is estimated that the patient lost over a foot during the evolution of the disease.

CASE VI.—After the preparation of the previous cases, I had the opportunity to observe an excellent instance of this disease in a colored man. This patient (C. B., Dispensary No. F. 4702), aged 61, came to The Johns Hopkins Hospital dispensary on April 7, 1913, complaining of pain in his right knee.

Family History.—The patient gives a negative family history: his father died when the patient was quite young; his mother lived to be 68 years old and was erect to the time of her death; none of his brothers or sisters was deformed.

Past History.—The patient, himself, has been unusually well all his life. He says that his legs were not bowed when he was a child. With the exception of measles and typhoid fever, he does not recall any infectious diseases. There is a history of repeated gonorrheal infections, but the patient denies having had lues.

Present Illness.—The present illness began 15 years ago, when the patient was 46 years old, with pain in the right knee and "rheumatism" in his right leg. Soon after the onset of these symptoms, his right leg began to weaken and to bend. According to the patient's account, the left leg remained unaffected until eight or nine years ago, when it too began to bend. He does not know whether his head has changed in size. At present he wears a No. 7¾ hat. The patient knows that he has gotten much shorter, but he cannot say how much he has lost in height.

In February of this year, the patient fell on his right knee. Since this accident he has been very much disabled. His rheumatic pains have become greatly aggravated and he can walk only short distances and then only with the aid of a cane.

Physical Examination.—April 19, 1913. The patient is a deformed, crippled, and dwarf-like colored man whose general posture is unusually simian in character. One is immediately struck by the enormous head and the extreme bowing of both legs. The head measures 64 cm. in its greatest circumference; the occipitofrontal diameter measures 21 cm. and the biparietal diameter measures 17 cm. The distance from tragus to tragus measures 43 cm. In this case, the enlargement of the calvarium in the parietal, occipital, and frontal regions is more striking than in the first three cases which I have been able to study. There is a large boss about the size of a hen's egg in the right frontal region. The face below the huge calvarium appears diminutive in comparison. The features are not enlarged.

Both lower extremities are bowed to such an extent that with the heels together, the distance between the two medial condyles of the femora measures 30 cm. The right leg is shorter than the left, but the latter shows more anterior bowing of the tibia. Both femora feel heavy and thickened; both show some outward bowing. The tibiæ are enormously thickened, nodular, and slightly tender on firm pressure. The anterior bowing is much more striking in this case than in the first three cases. The lower third of the left tibia is heavier, coarser, and shows the most anterior bowing.

In the upper extremities no marked changes are demonstrable. There is, however, obvious bowing of the left radius, and slight bowing of the right radius.

The thorax is emphysematous in type, the clavicles are a little thickened, but not strikingly so. There is no kyphosis or scoliosis of the spine.

The abdomen is full and shows no transverse furrow. The pelvis is not exceptionally wide, the measurement between the antero-superior spines and that between the iliac crests being 27.5 and 28 cm., respectively. Due to the marked bowing of the legs, the distance between the trochanters is increased to 35 cm.

Height.—The patient thinks that he was 5 feet 6 inches before the onset of his deformity. The grand expansion of the arms measures 69 inches. His present height is 61 inches. According to these figures he has lost between 5 and 8 inches in height.

Radiographical Study (Skiagram No. 17517. Reported by Dr. F. H. Baetjer).—There is osteoporosis of the head of the tibia with areas of bony thickening; the entire tibia is enlarged. The femur shows marked thickening, but no osteoporotic areas.

The patella is thickened and shows osteoporotic areas. There is a formation of osteophytes along the edge of the articular surface of the tibia, some of which have been broken off and are lying loose in the joint.

Skiagrams of the skull were not obtained.

HISTORICAL.

It is of some historical interest that studies of the skulls and bones collected in various archæological museums of the world would seem to indicate that the disease existed even in prehistoric days. Paget,* himself, made a careful study of the descriptions of large, thick, and porous skulls found in various museums. From a large number of specimens, many of them improperly classified, he was able to collect a group which are examples of true osteitis deformans. In 1885, Butlin [10] concluded from a study of the Neanderthal skull, thought by some to be rachitic, that the specimen belongs to the diseased condition now known as osteitis deformans.† From a study of Indian skulls and bones, Stegmann,[11] was able to report its presence frequently among the specimens observed. Wilks,[12] in 1857, observed some old specimens of this disease in the museum of Guy's Hospital. Recently, Waterhouse,[13] described a collection of bones dating from the year 1868, nine years before Paget's first communication, which are undoubtedly specimens from a case of osteitis deformans. This collection, presented to the Royal United Hospital in Bath by R. T. Gore, then surgeon to the hospital, is "from a man, aged 60, the subject of rickets in early life," and comprises a skull, scapula, clavicle, two humeri, a radius and ulna, femur, tibia, and fibula. These bones show very typical changes wrought by the disease which now goes by the name of osteitis deformans.

As a clinical entity, however, osteitis deformans is a disease of modern times. Certain cases reported prior to those of Paget as partial or local osteomalacia may have been atypical cases of the disease; as for instance, the cases mentioned by Paget: those by Saucerotte in 1801, Rullier in 1812, and Scoutetten [14] in 1841; whereas the cases described by Wrany in 1867, and by Wilks [15] in 1869 are considered by Paget, himself, as typical examples of the disease bearing his name.

* Ref. 1, p. 61.

† Jonathan Hutchinson (Illus. Med. News, 1889, II, 177) refers to a portion of a parietal bone taken from an Egyptian tomb and now in the museum of the College of Surgeons, which would appear to be a good specimen of osteitis deformans, and as such probably the most ancient on record.

The case of Wilks included by Paget as one of his five cases is probably the first good clinical picture of the disease recorded in the English language. The report of Wilks is entitled a "Case of osteoporosis, or spongy hypertrophy of the bones (calvaria, clavicle, os femoris, and rib, exhibited at the Society)." This communication was published in the Transactions of the Pathological Society of London, for 1869. In this report Goodhart, then house physician to Guy's Hospital, included an autopsy record of the disease in which he calls attention to some of the important pathological changes in the bones. Wilks,* l.c. in a letter to the *Lancet* in 1909, modestly calls attention to his description of the disease, and says that because he could find no new osseous tissue, he was not inclined to regard the condition as resulting from an inflammatory process.

Czerny,[16] in 1873, first introduced the term ostitis deformans for a case of rather acute inflammation of the lower part of the tibia and fibula occurring in a soldier 22 years of age, and associated with softening, bending, and hardening of the bones. A year later, Schmidt [17] and Volkmann [18] both used the term, the former in connection with a case of spontaneous development of curvatures of the tibia and femur, and the latter for a similar case in which the curvature was confined to the tibia. Whether these cases are to be regarded as cases of true osteitis deformans in the sense of Paget is still disputed. Paget,† himself, was not inclined to class Czerny's case with those described by him, and Fitz, in this country, is inclined to the view that "multiplicity of the bones affected is the constant characteristic."‡

Notwithstanding that much was known and written about osteitis deformans before Paget's description of the disease, we owe to him a masterly account of its important clinical and pathological features, as well as a differentiation of this affection from a host of other osteopathies: Osteoporosis, osteomalacia, rickets, and various forms of hyperostoses.

CLINICAL PICTURE

Some of the most important clinical features of the disease already have become apparent from the case records I have given. Paget's own description is so concise that I should like to quote him in this connection. In his original communication, he says of the disease:

"It begins in middle age or later, is very slow in progress, may continue for many years without influence on the general health,

* Ref. 12. He says: "I called the case 'osteoporosis' or spongy hypertrophy of the bones. I so named it because it was the word on the labels attached to some old specimens in the museum at Guy's, and which evidently belonged to a case of this disease, shown by the enormously thickened skull and the large, crooked, long bones of the limbs. In giving my lectures in 1857, I commented on these bones and said I did not think they arose from an inflammatory process because I could find no new osseous tissue, either on their surface or interior, and therefore, I considered the name to be most excellent. When, therefore, an example of the same disease came under my own notice, I called it 'osteoporosis,' and more especially as I discovered no new osseous tissue either as ostitis or periostitis—."

† Ref. 2, p. 225.

‡ Ref. 20, p. 401.

and may give no other troubles than those which are due to the changes of shape, size, and direction of the diseased bones. Even when the skull is largely thickened, and all its bones exceedingly altered in structure, the mind remains unaffected.

"The disease affects most frequently the long bones of the lower extremities and the skull, and is usually symmetrical. The bones enlarge and soften, and those bearing weight yield and become unnaturally curved and misshapen. The spine, whether by yielding to the weight of the overgrown skull, or by change in its own structure, may sink and seem to shorten with greatly increased dorsal and lumbar curves; the pelvis may become wide; the necks of the femora may become nearly horizontal, but the limbs, however misshapen, remain strong and fit to support the trunk. In its earlier periods, and sometimes through all its course, the disease is attended with pains in the affected bones, pains widely various in severity and variously described as rheumatic, gouty, or neuralgic, not especially nocturnal or periodical." *

Some of these clinical features have been emphasized by more recent writers. Latzko [25] maintains that the non-conformity between the anatomical changes in the skeleton and the retained ability to walk is pathognomonic of the disease. Fitz [26] emphasizes the multiplicity of the bones involved as a characteristic feature.

Later reports seem to indicate that the disease is not necessarily symmetrical. The disease may be more developed in the bones of one side of the body than in those of the other; or there may be a crossed involvement, as in the case of Levi [21] (a woman 62 years of age) in which the bones affected were: Left humerus and right radius; right femur and left fibula; whereas, both tibiæ were uninvolved.

Studies of the reported cases show that the skull, although the last to be involved, most frequently participates in the process, and that after the skull, the tibiæ are the bones most often affected. The latter are followed by the femora, pelvis, spine, clavicles, ribs, and radii.

Contrary to Fitz's assumption, Schirmer † [22] concludes from his collective study of the disease that there is a so-called "mono-osteitic" form, which for years may be confined to one bone, especially the tibia. In this group, Schirmer includes the cases reported by Schlesinger, Katholicky, Ménétrier and Gauckler, Schmieden and Symmonds.

According to the reported statistics, the occurrence of all of the six cases of this report in males would appear to be a mere coincidence. Most of Paget's 23 cases occurred in men. Of the cases collated by Packard, Steele, and Kirkbride, [l.c.] in which the sex was stated, 41 were in men, and 24 in women, that is 61 per cent of the cases occurred in males and 35 per cent in females. The more recent statistics of Schirmer, [l.c.] however, would seem to indicate that the disease was just as common in women as in men. Of 86 cases studied by him, 46 were in men and 40 in women.

With the exception of Cases III and VI in which the disease began in the fifth decade, in the four remaining cases the age of onset, as far as could be determined, was in the sixth decade. This corresponds closely to the age of onset of the largest number of recorded cases. Of the 86 cases analyzed by Schirmer, 28 cases came under observation between the ages of 50 and 60, and 25 between the ages of 60 and 70. In about 61 per cent of these cases the disease reached its full development in the sixth and seventh decades. In some of these cases the disease undoubtedly began earlier and of 25 cases in which the age of onset was stated, 17 began in the fifth and sixth decades. From these figures, it is obvious that osteitis deformans is a disease chiefly of old age.

The rheumatic pains usually attending the disease are not always present, or they may be so slight as scarcely to attract attention. This has lead Joncheray [23] to distinguish two varieties of osteitis deformans; a painful and a painless form. Cases II and IV of this report may be grouped under the painless variety. It will be recalled that in Case II the symptoms referable to arteriosclerosis and myocardial degeneration caused the patient to seek medical aid, and that he did not complain of any pain in the extremities. So also Case IV suffered from little pain. The symptoms in this case were arteriosclerotic in origin.

Interesting in this connection is the suggestion of Elting [l.c.] that the pains in the early stages of osteitis deformans may be due to distention of the periosteum, a view advanced by Durverney in 1757, in explanation of the pains in the initial stages of rickets. According to this view, the painless variety of the disease is due to its slow development. The periosteum in this instance being only gradually distended.

PATHOLOGY.

The more recent pathological studies of osteitis deformans have added little to our knowledge of the pathogenesis of the disease as described by Paget and Butlin. Some of the most fundamental problems of its pathology are still contended. Paget and Butlin believed the process to be inflammatory in nature. They based their conclusion upon a study of the histological picture, which shows changes associated with enlargement and with excessive production of imperfectly developed structures, and with increased blood supply. Stilling [24] believes that the primary process is a rarifying osteitis; and Higbee and Ellis [l.c.] from their careful pathological study state that resorption of bone appears to be the initial histologically recognized change. According to these writers, the reparative processes alone should be regarded as inflammatory in nature, which follow the resorption of bone, and which result in new bone formation.

However at variance writers may be regarding the initial step in the process, all who have studied the pathology of the osseous changes, describe a similar microscopic picture: essentially this consists of a resorption of bone associated with the excessive production of a poorly calcified bone designated as fibro-osteoid tissue.

Parkard, Steele, and Kirkbride picture the process as follows:

A. "Absorption of the compact substance causing enlargement and confluence of the Haversian canals. B. Formation of new bone which runs diffusely through the affected and the adjacent

* Ref. 1, p. 54.

† Ref. 22, p. 610.

healthy portions. This new bone remains uncalcified, and is in turn resorbed. C. The conversion of the medullary substance into a vascular connective tissue containing fat cells, giant cells, and leucocytes. In a small proportion of the reported cases cysts filled with gelatinous material and giant celled sarcomata occur in the medulla. D. As a consequence of these three processes, the ordinary relations of the compact substance and medulla are destroyed. The bones become exceedingly thickened and asymmetrical, but since the new bone tissue remains uncalcified, its elasticity permits of great deformity of the long bones from weight of the body, and fractures do not occur." *

Von Recklinghausen,[25] in particular, has emphasized the regressive changes of the fibrous marrow into gelatinous cysts, and the progressive changes leading to the formation in the long bones of small, brown, red tumors of the nature of giant-cell sarcomata. These, he regards as characteristic of a disease closely allied to Paget's disease, to which he has given the name of tumor-forming osteitis deformans (*tumorbildenden ostitis deformans*). Von Recklinghausen considers this condition as distinct from Paget's osteitis deformans, but Sternberg[26] contends that the two diseases cannot be differentiated histologically; clinically a point in the differential diagnosis is the comparative rarity in Paget's osteitis deformans of spontaneous fractures which are almost pathognomonic of the type described by von Recklinghausen.

On the other hand, the occasional occurrence of cases of osteitis deformans with tumor growth would appear to bring into close relationship the two types just considered. Collective studies of the reported cases have shown, however, that this relationship has been too strongly emphasized. Although Paget reports that of eight cases traced to the end five died with cancer or sarcoma, this is not true of the large number of cases recorded since then. Gruner, Scrimger, and Foster[27] state in a recent study of a case of Paget's disease with multiple sarcoma formation, that up to 1902, only 14 of the recorded cases were associated with tumor formation. Of these, four were carcinoma, five sarcoma, and four either carcinoma or sarcoma. Since 1902, and hence in more than one-half of the reported cases, Higbee and Ellis found mention of only two benign tumors.

What has been said of the microscopic changes observed in the bones of osteitis deformans helps to make clear the varied picture which these present in gross. As already mentioned, the two most important factors concerned in the production of the deformity are a temporary softening and a hypertrophy, followed usually by a progressive induration of the newly formed bone, so that after a period of years it may become of ivory-like hardness. This newly formed bone is at first soft, porous, and vascular, so that it yields when exposed to strain; but soon the process of new bone formation gains on the process of resorption and the bones thicken.

The bones of the calvarium may become markedly thickened, often measuring as much as 1.5 to 3.75 cm. (½ to 1½ inches) in the thickest portions. The shape of the long bones presents an appearance well described by Fitz:

"The surface is smooth or rough, nodular, or protuberant; the cortex thickened or thinned, spongy or eburnated; the cancellated structure sclerosed or coarsely trabeculated; the marrow spaces obliterated or transformed into cavities of various size. The central canal of the long bones is narrowed or dilated, even to disappearance, and the deformity of these bones is further increased by various degrees of abnormal curvature. There is no uniformity in the distribution of these alterations, and a single bone may give evidence of the decalcification, and absorption, the formation of osteoid tissue and its calcification, which are the processes concerned in the production of the gross changes.'

ETIOLOGY.

Our ignorance of the causation of osteitis deformans is nearly as great to-day as when the famous English surgeon first drew attention to it. In spite of the many carefully examined cases with pathological reports and radiographic studies, opinion is still much divided as to the exact nature of the condition. Many theories have been advanced. Heredity, syphilis, arthritis, and gout, trophic disturbances and the internal secretions have all been considered as causes. Each has found ardent supporters.

Heredity has long been supposed by some to be a determining factor in the etiology of the disease. Paget, himself, was not inclined to this view. In 1889, after he had seen 23 cases, he states: "I have tried in vain to trace any inherited tendences to the disease. I have not known it in two members of the same family. Many have had gouty ancestors, but I do not think more than any other equal number of persons in the same rank in life."[2] Since Paget, a considerable number of instances occurring in more than one member of the family have appeared in literature. I have been able to find about a dozen cases in which the affection existed in one or more members of the same family. Pick[28] reports the disease in father and daughter; Oettinger and Lafont,[29] in father and two sons; Smith,[30] in father and son; Chauffard,* in mother and daughter; Berger,† and Higbee and Ellis,[l.c.] in mother and son. It will be recalled that in Case III, of this report there was sufficient evidence for believing that the disease was present in the mother of the patient. Lunn,[32] and also Manwaring-White,[33] report the disease in two brothers,‡ Stahl,[34] in this country, and Parry,[35] in England, report the occurrence of the disease in two sisters, and Kilner,[36] in a brother and sister. The number of cases in which family tendencies existed is too small to justify any definite conclusions as to the part played by heredity in this condition.

Within recent years a number of French writers, notably among them Lannelongue[l.c.] and Fournier[37] have advanced the view that osteitis deformans is a late manifestation of hereditary syphilis, a form of syphilis hereditaria tarda. It is interesting in this connection that Paget, himself, states definitely that the disease is "not associated with syphilis,"§ for he was neither able to obtain a history of syphilis in any

* Ref. 5, p. 685.

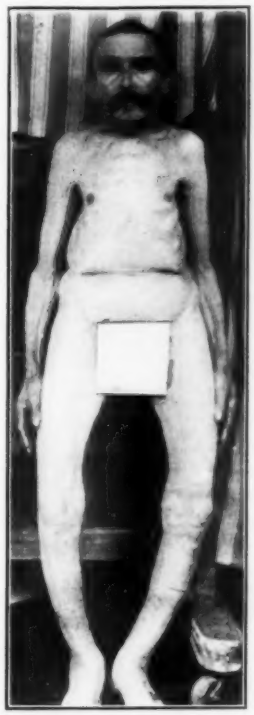
* Ref. 20, p. 401.

† Cf. Ref. 31. Lannelongue.

‡ Robinson (Trans. Path. Soc. Lond., 1887, XXXVIII, 262) reports the case of a clerk, æt. 52, whose brother about the same age suffered from the same disease.

§ Ref. 1, p. 55, 59.

CASE I.—Front view, showing general posture, broad pelvis, bowing of femora and of bones of forearm.



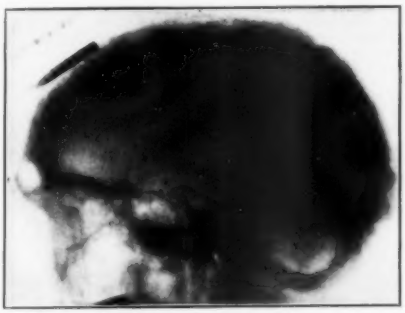
CASE IV.—View showing the simian attitude, the large head, flaring of ribs, transverse abdominal sulcus, and marked bowing of both femora and tibiæ.

CASE II.—View showing low stooping, round shoulders, and position of head far forward.

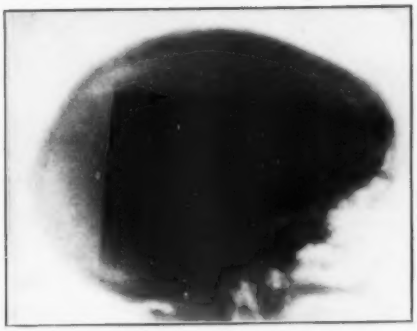
CASE III.—Patient at 53 years of age. View showing posture, large head and disproportionate length of arms. Height: 5 feet 3⅛ inches.

CASE III.—Skiagram of skull showing thickening of inner and outer tables with a flocculent deposit of bone irregularly placed over the entire outer table. Sella turcica slightly enlarged.

CASE III.—Patient at 28 years of age, showing erect posture. Height: 5 feet 7 to 8 inches.



CASE I.—Skiagram of skull showing a uniform deposit of new bone. Total thickness about one inch.



CASE II.—Skiagram of skull showing a uniform and symmetrical thickening of the bones. Thickness one-half inch.

CASE II.—Skiagram of tibia and fibula; tibia irregularly thickened with longitudinal areas of porosis; fibula shows little calcification, but longitudinal areas of porosis. Marked sclerosis of posterior tibial vessels.

CASE III.—Skiagram of tibia and femur showing thickening and small areas of porosis.

of the cases, nor could he demonstrate any known syphilitic changes in any of his patients.

The syphilitic nature of osteitis deformans is now largely discredited as a result of a more careful differentiation between the clinical and radiographic pictures of the two diseases. Clinically, the osteitis deformans of congenital syphilis may be differentiated from true Paget's disease by some of the points emphasized by Parkes Weber:[38] 1. The youthful age of the patients in the congenital syphilitic cases; 2, the relative absence of pain in those cases (here it is to be recalled that there is, according to Joncheray, a painless as well as a painful variety of osteitis deformans); 3, the favorable results obtained in the syphilitic cases under proper specific treatment; 4, in the syphilitic cases the tibiæ are most severely and most frequently affected. In Paget's osteitis deformans the disease not rarely first shows itself in one of the femora; 5, in the syphilitic cases, in addition to the general enlargement, the affected bones often present irregular bosses on their surface; 6, there is no evidence of any tendency for malignant tumors to supervene in the bones of the syphilitic cases, as there is in the bones of Paget's class of cases; 7, in the former class of cases there may be present other obvious signs of congenital syphilis.*

In 1902, Kienböck[39] showed by careful studies of radiograms of syphilitic bone affections and of Paget's disease that radiographically the two diseases could be differentiated. More recent comparative X-ray studies of the bones in osteitis deformans, hereditary syphilis, and osteomalacia by Legros and Leri[40] would seem to point in the same direction.

Another theory has for a time held sway and still finds adherents; viz., that which attributes the changes to trophic disturbances under the influence of the nervous system.† We know, for instance, that in certain diseases such as tabes, syringomyelia, and at times in diseases of the anterior horn cells, bony changes, often advanced, may be met with, and in a number of instances of Paget's disease diffuse alterations have been found in the spinal cord (two cases of Gilles de la Tourette and Marinesco,[41] and the case of Lévi[42]). But they have never been sufficiently definite or frequent enough to find a causal connection between them and the bony changes observed in Paget's disease.

Some writers, basing their views upon the experience of Schiff,[1.c.] who was able to produce trophic changes in the bones of dogs (thickening of the tibia, fibula, and bones of the feet) by section of the sciatic and crural nerves, believed that the bony changes of Paget's disease are due to lesions of peripheral nerves. Schirmer ‡ dismisses this view as carrying little weight, since in such experiments an atrophy of bones similar to senile atrophy is produced.

Furthermore, the theories which associate osteitis deformans with gout on the one hand, and arthritis deformans on the other, have little to support them. The gouty theory is based largely upon the occurrence of so many cases of the disease in England, "the land of the gout," and upon the coincident presence of the disease in gouty individuals. According to Joncheray,[1.c.] up to 1893, 40 of the 60 cases which showed this association were reported from England. As is pointed out by Higbee and Ellis,[1.c.] however, England no longer has a preponderance of the cases. Of the 90 cases they collected from the years 1901 to 1911, only 13 occurred in England. Among the American cases very few were associated with gout.

Again, the view of Lancereaux,[43] and of Richard,[44] has met with little support. These writers regard osteitis deformans as part of the same morbid process which gives rise to arthritis deformans. Although it is possible to find some instances in which the two diseases have coexisted, there seems to be little reason for assuming any relationship between them.

Probably the most recent, interesting, and stimulating view is that which regards osteitis deformans as the result of a faulty metabolism, due to a perversion of the internal secretions. It is natural that the recent additions to our knowledge of the influence exerted by the hypophysis and the parathyroids in calcium metabolism should have called forth such views. The very recent work of MacCallum and Voegtlin[45] on tetany has especially emphasized the connection between the parathyroid secretion and the calcium exchange in the body.

Higbee and Ellis,[1.c.] in their excellent communication on this disease present an interesting discussion of this view. These authors have been able to find only one reported case in which the hypophysis in osteitis deformans showed any definite change. This is the case of Bartlett,*[46] who interprets the preponderance of large polygonal (chromophile cells) over the small cuboidal cells of the anterior lobe as a sign of increased functional activity of the gland. In the autopsy records of his second case, Stilling[1.c.] described the hypophysis as soft, flabby, depressed and cyst-containing, and the posterior part of the sella and clivus as considerably raised; and Grumer, Scrimger, and Foster[1.c.] report an atrophy of the pituitary gland. In all the other recent reports in which this gland was studied, it is reported as normal. In only one of three of the cases of this report, in which skiagrams of the skull were obtained was the sella turcica larger than normal.

Whereas the thyroid gland was found sclerotic in three of the recorded cases (Lévi,[1.c.] Hudelo and Heitz,[47] Higbee and Ellis[1.c.]), little or no mention is made of the parathyroids. The association of osteitis deformans with an apparent absence of parathyroid glandules, which Higbee and Ellis report, would seem to be unique in literature. They found in the thyroid gland little islands of cells suggestive of parathyroid tissue. On the basis of this observation, they conjecture that an actual metaplasia of thyroid into parathyroid tissue may have occurred and that this parathyroid tissue was assuming the function of the absent or atrophied parathyroids.

Regarding the metabolism of osteitis deformans little is

* Ref. 38, p. 86.

† Dr. Morton Prince, of Boston, strongly supports this view. (Tr. Ass. Am. Phys., 1902, xvii, 392.)

‡ Ref. 22, p. 694.

* Pp. 374, 375.

known. Paget reports the results of a chemical analysis of portions of the diseased skull and tibia of his case, and of a healthy tibia in comparison with them. These analyses showed a reduction of the inorganic salts and phosphoric acid in the skull and tibia and the presence of fat which is absent in normal bone. The reduction in the magnesium salts was confirmed by Gilles de la Tourette and Marinesco and by Ménétrier and Gauckler.* Higbee and Ellis state that the recorded urinary analyses show a varying output of calcium salts in this disease.

It would appear from these few observations that in the present state of our knowledge the assumption of a causal connection between the internal secretions and osteitis deformans is mere speculation; but as Higbee and Ellis point out, the metabolic processes in this disease are very little understood and it may be that accurate metabolic studies in osteitis deformans will help to solve the problem of its causation.

In conclusion, I desire to express my thanks to Dr. F. H. Baetjer for the interpretation of the X-ray plates, and to Dr. Louise Pearce for her assistance in photographing the patients.

REFERENCES.

1. Paget: Med.-Chir. Tr., 1877, LX, 37.
2. ———: Ibid., 1882, LXV, 225.
3. ———: Illus. Med. News, 1889, II, 181.
4. Higbee and Ellis: J. M. Research, 1911, XIX, 55.
5. Packard, Steele and Kirkbride: Tr. Ass. Am. Phys., 1901, XVI, 666.
6. MacPhedran: Med. News, 1885, XLVI, 617.
7. Watson: Johns Hopkins Hosp. Bull., 1898, IX, 133.
8. Elting: Ibid., 1901, XII, 343.
9. Osler: The Principles and Practice of Medicine, 1912, 1144.
10. Butlin: Lancet, 1885, I, 519.
11. Stegmann: Wien. klin. Wchnschr., 1905, XVIII, 619. Discussion.
12. Wilks: Lancet, 1909, II, 1627.
13. Waterhouse: Lancet, 1907, I, 1215.
14. Scoutetten: Gaz. méd. de Paris, 1841; quoted by Patscher: Ueber deformirende ostitis. Dissert., Berlin, 1880.
15. Wilks: Tr. Path. Soc. Lond., 1869, XX, 273.
16. Czerny: Wien. med. Wchnschr., 1873, XXIII, 894.
17. Schmidt: Arch. f. Heilk., 1874, XV, 81.
18. Volkmann: Beitr. z. Chir., 1875, 148.
19. Latzko: Wien. klin. Wchnschr., 1905, XVIII, 708.
20. Fitz: Tr. Ass. Am. Phys., 1902, XVII, 398.
21. Levi: Bull. Soc. anat. de Par., 1896, No. 13,439.
22. Schirmer: Centralbl. f. d. Grenzgb. d. Med. u. Chir., 1908, XI, 561, 609, 641, 689, 721. (Exhaustive review of literature up to 1908.)
23. Joncheray: De l'ostéite deformante. Thèse, Paris, 1893.
24. Stilling: Virchow's Arch. 1890, CXIX, 542.
25. Von Recklinghausen: Festschr. d. Assistenten f. Virchow, 1891.
26. Sternberg: Nothnagel's Spez. Path. u. Ther., 1899, VII, p. 64.
27. Gruner, Scrimger & Foster: Arch. Int. M., 1912, IX, 641.
28. Pick: Lancet, 1883, II, 1125.
29. Oettinger & Agasse-Lafont: Nouv. Icon. de la Salpétrière, 1905, XVIII, 292.
30. Smith: M. Soc. Tr., London, 1905, XXVIII, 324.
31. Lannelongue: Bull. Acad. de méd., 1903, XLIX, 299. (Discussion.) Quoted by Emerson, Osler's Mod. Med., 909, VI, 718.
32. Lunn: Trans. Clin. Soc., London, 1885, XVIII, 272.
33. White: Brit. M. J., 1909, II, 12.
34. Stahl: Am. J. M. Sc., 1912, CXLIII, 527.
35. Parry: Brit. M. J., 1912, I, 879.
36. Kilner: Lancet, 1904, I, 221.
37. Fournier: Bull. Acad. de méd., 1903, 3 s., XLIX, 532. Quoted by Emerson, Osler's Mod. Med., 1909, VI, 721.
38. Weber: Brit. J. Children's Dis., 1908, V, 83.
39. Kienböck: Ztschr. f. Heilk., 1902, XXIII, 130.
40. Legros & Leri: Soc. Neurol. Par., 1908, Nov. 5.
41. Gilles de la Tourette & Marinesco: Nouv. Icon. de la Salpétrière, 1895, VIII, 205.
42. Lévi: Nouv. Icon. de la Salpétrière, 1897, X, 113.
43. Lancereaux: Traité de l'herpétisme, Paris, 1883, 343. Quoted by Schirmer.
44. Richard: Contribution à l'étude de la maladie osseuse de Paget. Thèse, Paris, 1887, No. 282. Quoted by Schirmer.
45. MacCallum & Voegtlin: J. Exp. M., 1909, XI, 118.
46. Bartlett: Yale M. J., 1910, XVI, 367.
47. Hudelo & Heitz: Nouv. Icon. de la Salpétrière, 1901, XIV, 415.

* Ref. 22, p. 691.

DIABETES IN EARLY INFANCY.

By J. H. Mason Knox, Jr., M. D.,
Associate in Pediatrics, The Johns Hopkins University.

Diabetes mellitus is a disorder of nutrition, in which grape sugar accumulates in the blood, and is excreted over long periods in the urine even when only moderate amounts of carbo-hydrates have been ingested. This condition, always serious, is found most frequently in middle life. Thus in an elaborate tabulation based on French, English and German statistics, Lapine[1] found that 74 per cent of all cases occurred between 30 and 60 years of age, that but 2 per cent of the incidence of this disease took place between 1 and 10 years, and but 13 per cent before 30 years.

Among six thousand four hundred and ninety-six (6,496) fatal cases of diabetes occurring in England and Wales in ten years, 1861-1870, there were but eight under 1 year.

The condition would appear, therefore, to be among the rarest affections in early infancy.

This lends some interest to the following report of an instance of diabetes mellitus in an infant during its first year.

Case A. P.—An infant girl, white, 9 months of age.

Family History.—Mother is well and a highly strung nervous woman. She had had an attack of rather severe jaundice two years before. The father, at present in good health, limps from healed tuberculosis of the hip. One sister aged four years is well. One brother died at four months, in the summer about two years ago, from gastro-intestinal disorder. There is no history of diabetes,

syphilis, or malignant disease in the family, and no other history of tuberculosis.

Past History.—The child's birth was normal; she was breast-fed with the addition of one or two bottles of diluted cow's milk for several months.

At four months she had a severe attack of bronchitis, during which the urine was found to contain pus cells, which, however, disappeared after the administration of urotropine. Several examinations of the urine, during the following months, showed it to be normal, containing no trace of sugar. At five months the child had some digestive disturbance and was put on malt soup mixture. She thrived for a time and gained rapidly in weight. She was first seen by the writer when she was about seven months of age; then she appeared to be perfectly well. Inquiry elicited the information that the child was receiving an unusually large amount of malt soup in her milk mixture, certainly over 10 per cent. This was discontinued and a simple milk mixture substituted, consisting of ⅔ milk, ⅓ water and 4 per cent dextrimaltose. The child did well for a month and then was seen on May 26, 1912, by my associate, Dr. H. L. Whittle, because she was not gaining in weight. At this time the physical examination was negative. The child was bright, but seemed rather irritable. The skin was dry and clear. Weight 19¾ lbs. There was no fever. Four days later, May 30, the child was found to have a temperature of 101° F. There was a definite "fruity" odor to the breath. She had lost 1½ lbs. Examination of the urine showed it to contain between 4 per cent and 5 per cent of glucose. Acetone was present. There was no diacetic acid and but a trace of albumen.

The following day the child was put on *Eiweiss* milk. Weight had fallen to 17 15/16 lbs. The temperature was 99.4° F. The sugar content of the urine diminished under this diet to 2 per cent and two or three days later to 1.5 per cent. The general condition of the child was not satisfactory and on June 7 she was admitted to The Johns Hopkins Hospital on the service of Dr. Barker, through whose courtesy I have the opportunity of reporting the case. Shortly after her admission the child apparently tired of *Eiweiss* milk. The amount of acetone in the urine increased and the diet was changed to a mixture of 32 per cent cream, albumen and water, the mixture having a composition of about 3 per cent fat, 4 per cent sugar and 2 per cent proteid. On this the weight remained unchanged for several days. The condition of the urine is indicated in the following table:

June.....	8	9	10	11	12	13	14	15
Acetone.....	0	0	Trace.	Trace.	Trace.	Mod. Amt.	+	+
Diacetic acid..	0	0	0	0	0	0	+	+
Sp. gr.....	1018	1014	1016	1010	1013	1010	—	1025
Total urine....	200+	Not det.	160+	370	+	—	—	0
Sugar per cent.	.5	.4	.4	.4	.6	.8	1.6	4.4
Amount.....	1 gram	.7	.64	2.5 12 hrs.	1.8	.12	....	....

Each examination of the urine gave a strong, reddish precipitate with Fehling's solution, a black precipitate with Nylander's, a positive fermentation test and dextro rotation with the polariscope. Several examinations of the stools for sugar were negative.

A week after admission the patient became drowsy and refused nourishment. Increased amounts of acetone and diacetic acid were found in the urine. The cream mixture was changed to a whole-milk mixture to increase the amount of lactose and ward off the impending coma. A sodium bicarbonate 4 per cent solution was given by rectum and by gavage. There was no permanent improvement, the patient became more and more comatose, respirations were deep and sighing in character, and there was considerable nausea. The temperature rose and there was some evidence of pulmonary involvement. The urine throughout did not contain albumen or form elements.

The patient died eleven days after admission and after a recognized illness of about three weeks.

Autopsy No. 3742.—Performed four hours after death. Dr. Winternitz.

Clinical Diagnosis: Diabetes Mellitus.

Anatomical Diagnosis: Bronchopneumonia and cloudy swelling of viscera. Skin and mucous membranes pale. There were a number of scattered areas of bronchopneumonia in both lungs, more marked in the right.

Heart: Normal.

Pancreas: Was of normal size, somewhat triangular in shape, firm, of an ivory-gray color, and showed no excess of fibrous tissue on cross section. Lobules were homogeneous in appearance. Here and there very small spots were seen, apparently islands of Langerhans. The other viscera showed no macroscopical changes, except that the kidneys preserved their fetal lobulation. The cortex of each kidney was pale in contrast to the pyramidal portion which was much congested.

Microscopical Examination.—The thyroid showed some evidence of increased functional activity, in the misshapen acini and the high cubical cells lining them. A few of the alveoli were large, round and full of colloid.

Sections of the pancreas showed the lobules to be separated from each other by rather broad septa, which consisted principally of very loose connective tissue. There were many small round cells in the interstitial tissue, which in some places seemed to replace the acini. The connective tissue was increased. The islands of Langerhans were diminished in size and number. In one section none were seen. The capsule was thickened and in the connective tissue trabeculæ were visible.

We have presented, therefore, a case of diabetes mellitus of probable pancreatic origin in an infant.

The points I should like to emphasize especially are the age of the patient, 9 months; the insidious onset, but rapid progress of the disease, three weeks of symptoms; the marked loss in weight, 2 pounds in 5 days; the absence of greatly increased thirst or hunger; the moderate polyuria; the early appearance of acidosis and coma and the negative findings at autopsy, except as concerned the slight but suggestive alterations in the pancreas.

I have attempted in the time at my disposal to collect the reported cases of diabetes *under one year* of age with the hope that some inferences can be drawn concerning this unusual but dangerous malady as it appears in early infancy. The number of cases in children *over* twelve months of age is of course considerably larger, as the incidence of the disease increases slowly with age until the third decade.

It seemed wise, however, to set an arbitrary age limit of one year to call attention to the occurrence of the malady in earliest infancy, when it is rarely suspected and often difficult to recognize, and because, too, diabetes in later childhood takes on the familiar features of the diabetes in adult life. (See table annexed.)

I am aware that the tabulation leaves much to be desired—that the urinary examination in the majority of instances is unsatisfactorily reported. The amount of urine in 24 hours is almost never given, doubtless partly because of the difficulty of obtaining it, and, of course, the more modern and selective tests for glucose were not applied in the examination of the early cases. Allowance being made for these unavoidable defects, a study of the clinical features and the results of treatment in the sixteen cases included in the table would suggest that they probably were cases of real diabetes, *i. e.*, that they exhibited a nutritional disturbance associated with

sugar (probably glucose) in the urine, persisting even when moderate amounts of carbo-hydrates have been ingested.

A second series of eleven cases, most of them reported as diabetes, but concerning the real nature of which there is much more uncertainty, have been omitted as "Doubtful Cases." In some the data were too fragmentary; others were probably cases of alimentary glycosuria. Concerning these no deductions can be drawn.

We are indebted for reference to some of the earlier cases to the collective investigation of Kulz[2] 1878, Stein[3] 1890, and of Wegeli[4] 1895. These writers have together reported upwards of three hundred diabetes cases in children under fifteen years of age. Of this number six have been included in our series as real diabetes during the first year and four others were classed as "doubtful."

Incidence.—The disease, although still, of course, very unusual in infancy, seems to be becoming more frequent. In more than forty years (1852 to 1896) but seven cases could be found reported, while the condition has been described in at least nine babies in the last fifteen years.

Sex.—Among adults it is well known that men are more frequently afflicted with diabetes than women in proportion of two to one or three to two, according to different investigators. This disproportion between the sexes does not seem to apply to diabetes occurring under 15 years, as the cases tabulated by Kulz, Stern, and Wegeli, above referred to, are about equally divided between boys and girls. In our series of 16 cases in early infancy the sex is given in 14 instances. Of these babies 11 were male and 3 female. Probably but little importance should be attached to this inequality between the sexes, as it is likely that a larger proportion of cases in girls was missed because of the difficulty of obtaining specimens of urine.

Age.—The babies in our series can be divided into two general classes, according to their age at the beginning of symptoms, namely, those in which the condition was noticed within a few days after birth (3 cases), and those in which several months elapsed, usually five or more, before the disease was recognized (13 cases). The cases are too few to admit of theorizing, but they suggest that the defect in the carbohydrate assimilation, though it be congenital, may not be more severe than when the disease begins a little later in infancy, for one infant (No. e), in which definite symptoms with glycosuria were discovered shortly after birth, recovered and another one (No. a) lived for at least eight months.

Family History.—In but half of the cases is there any statement as to the family history. In three instances it was good throughout; in three a grandparent or a great-aunt had had diabetes; in two there was an indefinite tuberculous family history. In one of the "doubtful" cases two older children in the family had the same condition as the 3-months-old baby, which was, however, almost certainly alimentary glycosuria.

Causal Factors.—In four instances there are no suggestions offered as to any possible cause for the condition.

Of the twelve remaining cases in six instances the condition seems to have followed an injury to the central nervous system. In two of this group (Nos. b and g) the patients, aged 7 and 10 months, respectively, sustained a severe fall, striking the head; this was followed in one case by repeated convulsions and in the second by continued restlessness and a sharp rise in temperature. In two other instances belonging to this general group the symptoms may have been associated with injury at birth, as the labors were described as difficult, one (No. h) being a face presentation, the other (No. p) resulting in a head abrasion, which required six weeks to heal.

It would be interesting to follow the urine of a series of babies born after protracted and difficult labors to determine whether in them a larger proportion of transient glycosuria or diabetes mellitus develops than in the average baby.

The four remaining instances were associated either with increased cerebral pressure or deformity of the brain—hydrocephalus (Nos. d, k and m) and encephalus (No. n). It is not my purpose to discuss in this connection the neurogenous theory of diabetes or whether injury to or pressure upon the central nervous system can produce diabetes independently of the pancreas. As is well known, Von Noorden[5] holds that all these cases are either transitory non-diabetic glycosuria or true pancreatic glycosuria affected by nervous influences. In any case the appearance of persistent glycosuria following mental shock or injury to or disease of the brain or spinal cord is a well-recognized sequence and the proportion of these cases seems to increase inversely to the age of the patient. In one case (No. i), in which the onset was insidious and the conditions, although alarming for a time, ended in recovery, the author considers the disease to have been due either to irritation of the central nervous system, the result of painful dentition, or an arrested development of the pancreas. Neither of these explanations seems satisfactory. In three other cases, our own included, the beginning of the symptoms followed an unusual amount of sugar in the diet. One baby (No. f) was fed on condensed milk, another, that of Langstein (No. o), received 150 grams of sugar in addition to a liter of milk, that is, about 200 grams daily; and in my own case, as already pointed out, about a liter of milk was given, containing 10 per cent malt soup. A number of writers, including Griesinger, Cantani and Naunyn, are quoted by Langstein *[m] as favoring this cause for certain cases of diabetes. It would appear a little suggestive that, in the case cited by Langstein and in my own, definite diabetes mellitus should arise in previously well babies 8 months of age, both of which had been given an unusually large daily amount of sugar.

Symptoms.—The majority of the cases of the series showed several symptoms in common. At first, restlessness was usually noted; this was followed by increased thirst and hunger and the passage of a larger amount of urine; loss of weight was a prominent symptom wherever the descriptions are adequate.

Multiple abscesses were present in two cases (Nos. b and f); gangrene of the lung in one (No. d); sore over the sacrum

* See bibliography to table of cases.

No.	Observer.	Date.	Sex.	Age.	Family History.	Causal Factors.	Symptoms.	Urinary Findings. Sugar.				Duration of Illness.	Result.	Diet and Treatment.	Autopsy Findings.
								Sp. Gr.	Variety	Per Ct.	Total Qnty.				
a.	Kitselle.....	1852	M.	A few days.	? Not stated.	?	Restlessness, thirst, hunger, constipation, polyuria, loss of weight, urine sweet like honey, napkins sticky. After 8 months urine offensive.	?	....	?	Large	8 months.	Died.	Breast milk, semmel tea, bread and water, Dovers powder.	.....
b.	Rossbach	1874	F.	8 months.	? Not stated.	Fall on head at 7 mos. Severe contusion of brain.	Repeated convulsions after fall, followed by unconsciousness, vomiting, subnormal temperature, irregular respiration, cyanosis, thirst, polyuria, furunculosis, emaciation.	?	Glucose	2–10	Large	3 months.	Died.	Diluted milk and cream broth.	Left kidney slightly enlarged, brain and pancreas not examined, cloudy swelling.
c.	Busch.....	1876	?	Under 1 year.	Unknown.	?	Restlessness, great thirst, emaciation, coma, ending in death.	1025	Glucose	5	?	23 days.	Died.	Nothing given.	.....
d.	Hagenbach	1879	M.	8 months.	Not stated.	Hydrocephalus.	Great thirst, marked polyuria. After 13 months gangrene of lungs.	1036	Glucose	+ ?	Large	13 mos.	Died.	Milk diet, salicylic acid.	Gangrene of lungs, chronic hydrocephalus.
e.	Garnerus	1884	M.	A few days.	Good.	Congenital or possibly from chill following bath.	Restlessness, hunger, thirst, polyuria.	1010	Glucose	+ ?	Large	2 months.	Recovery.	Milk with oatmeal water, buttermilk with ½ glycerine. On this the glycosuria disappeared.	.....
f.	Nichuas	1891	M.	3 months.	Grandfather died of diabetes.	Fed on condensed milk.	Polyuria, abscesses.	....	?	2–3	Large	?	Died.	Condensed milk.	.....
g.	Tavaria.....	1893	M.	10 months.	Parsi Indian.	Fell from cradle.	Shortly after fall, elevation of temperature, restlessness, thirst, dyspnea, flies attracted to napkins.	?	Glucose	+ ?	Large	2 weeks.	Died.	Breast milk, diluted milk.	Pneumonia.
h.	Bell	1896	M.	3 months.	Father's aunt died of diabetes, and mother's grandfather of tuberculosis.	Difficult labor. Face presentation.	Restless, thirst, polyuria, fruity odor to breath, eczema, coma.	?	Glucose	+ ?	Large	Several days.	Died.	Breast milk, skim milk diluted.	Nothing abnormal.
i.	Caillot	1900	F.	5 months.	Good.	Painful dentition.	Edema, restlessness, hunger, thirst, polyuria.	?	Glucose	1.5[1]	Large	3 weeks.	Recovery.	Breast milk suggested arrested development of pancreas.	.....
k.	Orloff.....	1901	M.	5 months.	Not stated.	Hydrocephalus.	Restlessness, hunger, thirst, polyuria, loss of weight, sore on sacrum.	?	Glucose	+ ?	Large	Several days.	Died.	Not stated.	Dilatation of lateral ventricle.
l.	Young	1901	M.	6 months.	Foundling.	?	Restlessness, indigestion, vomiting, dry skin, fever, polyuria.	1030	Glucose	5	Large	1 month.	Died.	Pasteurized milk mixture, 4% fat, 7% sugar, 2% proteid.	Both kidneys greatly enlarged, "parenchyma inflamed."
m.	Langstein.....	1909	M.	6 months.	Not stated.	Chronic hydrocephalus.	Repeated convulsions. No intestinal disturbance.	?	Glucose	0.1–1	.....	A few months.	Died.	Not stated.	Internal hydrocephalus.
n.	Langstein.....	1909	M.	7 days.	Not stated.	Anencephalus.	No intestinal disturbance.	?	Glucose	+ ?	.....	9 days.	Died.	Breast fed.	Complete lack of cerebral hemispheres.
o.	Langstein.....	1909	M.	8 months.	Good.	Excess of sugar in diet 150 grams + 1 liter of milk.	Some intestinal disturbance, thirst, hunger, loss in weight, skin dry, acetone present.	?	Glucose	6–10	Large	Several months.	Apparently well.	Cows milk diluted, then casein and cream mixture, then oatmeal gruel plus small quantities casein cream mixture bouillon and green vegetables, sodium and bicarbonate.	.....
p.	Eaton and Woods	1911	M.	6 months.	Mother's mother died of diabetes.	Labor instrumental and difficult; abrasion of head.	Two toes red and swollen, napkins sticky, thirst, polyuria, acetone present.	1035	Glucose	6–10	Large	2 years.	Died after 2 years.	Breast fed, washed cream mixture plus broth.	.....
r.	Knox	1913	F.	8 months.	Father had tuberculosis of hip.	Excess of malt soup (almost 10%) + 1 liter of milk.	Loss of weight, skin dry, drowsiness, acetone, sighing respirations, coma, fever.	1010 to 1035	Glucose	05[1]–45	Large	3 weeks.	Died.	Milk mixture plus maltose, Eiweiss milk cream albumin mixture.	Diminution in number and size of islands of Langerhans, bronchopneumonia.

in another (No. k). At least three cases ended in coma (Nos. c, h, and r). Acetone was noted in the breath or the urine in four instances (Nos. h, o, p, and r).

Thirteen cases died; three apparently recovered. The first two of these cases were definitely milder in type; the last, reported by Langstein, though not of the severest type, was probably helped by prompt and efficient therapy. Whether the condition will return or not is uncertain.

The Duration of Illness.—As may be expected, the length of time from the beginning of symptoms to their termination, either in sugar-free urine or in death, is very variable, depending largely upon the severity of the disease. The majority of the more rapid cases terminated in three weeks; one of them (No. h) in several days. Eaton's case lived for two years, and others survived several months.

Urinary Findings.—As has already been intimated, the urinary findings in the earlier cases are very incomplete; the diagnosis rests upon the finding of sugar, presumably glucose, which ferments with yeast and precipitates Fehling's solution, and upon the general symptomatology. In the last three cases glucose was definitely demonstrated in the urine by the phenylhydrazin test (Fisher).

The average specific gravity of the urine in the six cases which have been recorded is high for the urine of infants, being from 1010-1036. The amount in 24 hours was in every case large, but was only measured accurately in the case of Langstein (No. o), when in one 24-hour interval 680 cc. were passed. There is a record of the percentage of sugar in individual specimens in nine cases; it varied from 1 to 10 per cent. In nearly every instance the precipitate with Fehling's solution is described as abundant; albumen was practically never present in any considerable amount; and formed elements were not described. It is interesting that attention was drawn to the condition of the urine in several instances by the stiffness of the napkins after drying. In the Indian case (No. g) the collection of flies on the napkins first aroused suspicion. In an older child the white sugar remaining upon the floor, where the child had voided, suggested the nature of the malady.

It has, of course, long been known that the mere presence of glucose, even in considerable quantities, in the urine of infants does not establish the diagnosis of diabetes. As Grisz[6] and many others have pointed out, reducing substances are frequently found in infants' urine, and in cases of gastro-intestinal disorders, for example, lactose or a cleavage product of it is frequently present, even in the urine of breast-fed infants. The limit of assimilation for milk sugar is, in normal infants, about three grams per kilo of body weight, and this amount is greatly reduced in many intestinal disorders. In certain toxic conditions it is asserted by Helmholtz[7] that one-hundredth of the amount of lactose assimilated by a normal child may produce lactosuria.

Aschenheim[8] has shown that the tolerance to grape sugar also varies greatly in certain other conditions. For example, in eczema the tolerance may fall to .75 of a gram per kilo body weight, and he considers that from 80 to 85 per cent of eczematous infants have glycosuria when taking the normal diet. Cobliner[9] has recently pointed out that the percentage of sugar in the blood of infants averages 0.119 per cent, a considerably higher content than that of adult blood, which contains, according to Leifmann and Stern,[10] about 0.085 per cent. Children with exudative diathesis have hyperglycæmia, associated, as we have seen, with a lowered tolerance; while in the decomposition or atrophy there is hypoglycæmia. It is, therefore, necessary in making a diagnosis of diabetes in infancy to consider both the condition of the patient, the diet, the probable carbo-hydrate tolerance and the amount of sugar in the urine when the patient is taking a carbo-hydrate free diet.

Diet and Treatment.—But little can be learned from the consideration of the diet and treatment of the early cases; most of them received milk in some form; several of them breast milk. In one case (No. b) the glycosuria was reduced by diluting the milk mixture and adding cream. In another (No. e) a diet of butter milk and the administration of salicylic acid in large doses is said to have decreased the urine and the sugar output. In the last three cases of the series, those of Langstein, Eaton and my own, a definite effort was made to reduce the sugar of the milk mixture. Langstein's case is particularly instructive. His patient, 8 months of age, was given a milk mixture, two parts of milk, one part of water, about 1300 grams in 24 hours, divided into 5 feedings. This diet contained about 40 grams of sugar. There was excreted in the urine at this time from 6 to 8 per cent of glucose, the kind of sugar being accurately determined. No acetone nor diacetic acid was present. The attempt was made to render the urine sugar free by feeding the small patient a milk mixture from which the lactose was to a large extent removed. It was prepared as follows:

The casein of a liter and a half of milk precipitated by rennin was collected in a cloth and thoroughly washed. It was then passed through a fine sieve into a mixture of 200 grams of cream and 1300 grams of water and sweetened with saccharine. On this diet the sugar content of the urine fell to about 8 grams a day, approximately the quantity furnished in the mixture. Under these conditions, however, acidosis quickly developed, the ammonia co-efficient increased 33 per cent, corresponding to a quantity of about 1.4 per cent of ammonia excreted.

The child became somnolent, apathetic and without appetite. Five grams of sodium bicarbonate were given daily without producing much change in the condition. At this time a liter of thick oatmeal gruel was introduced by a stomach tube in five feedings on each of two succeeding days. This was followed by a marked improvement in the patient's symptoms. The urine became sugar-free and the acetone bodies quickly disappeared. A small quantity of milk mixture was now carefully added as follows:

The curd from a liter of milk and 100 grams of cream were suspended in 900 grams of oatmeal gruel and given in 24 hours. The quantity of cream was gradually increased; when it reached 300 grams sugar again appeared in the urine, 4 to

5 per cent in 600 or 700 cc. of urine. Again an oatmeal gruel day was substituted and in addition a little bouillon and a green vegetable were added to the modified milk mixture. In this way the sugar tolerance of the infant was increased until it could take 16 grams of milk sugar in addition to the carbo-hydrate gruel without any glycosuria or acidosis; an increase of the sugar intake beyond this point was always followed by glycosuria. On this diet there was no loss in body weight and at the close of the report the child was doing well, although its ultimate recovery is of course uncertain.

I have gone into the details of this case because it is unique in the literature and also for the reason that it shows well how the dietetic measures which have been more or less successful for many years in combating the progress of diabetes in adults can be made applicable in the treatment of the same condition in infants. The remarkable results following the so-called oatmeal cure are not at present thoroughly understood. It has been shown, however, by Czerny and Keller that the milk sugar is better assimilated when it is given together with the second carbo-hydrate in the form of a cereal mixture, but this fact does not explain the greatly increased value of oatmeal gruel as compared to other cereals.

In Eaton's case an improvement was noticed after the administration of washed cream in addition to the breast milk; this was prepared by taking the cream off a quart of milk, shaking it with an equal quantity of water, and, after the cream had again risen, making a mixture of one part cream to four parts water; to this a little saccharine was added. An analysis of the mixture is not given, but it contained, of course, comparatively little lactose. The child was given 51 oz. of the mixture several times a day. Although the sugar in the urine of this child was unquestionably grape sugar, and acetone and diacetic acid were frequently present, there was no suggestion of coma and the case was evidently one of comparatively light severity.

In our own case, when the glycosuria was discovered an attempt was made to reduce the carbo-hydrate of the food by the use of *Eiweiss* milk, having a sugar content of about 2 per cent. This was successful for a few days only, when the child became somnolent and the acetone bodies increased markedly in the urine; notwithstanding the exhibition of large quantities of sodium bicarbonate and an increased amount of carbo-hydrate, the case went on to a rapidly fatal coma.

Autopsy Findings.—Partial post mortem examinations were made in nine instances and add little to our knowledge.

Hydrocephalus was described in three cases and a gross defect in cerebral substance in a fourth, as had been noted during life. In our case alone was there any microscopical examination of the pancreas. In this, as above described, there was apparently a reduction in number and size of the islands of Langerhans. The importance of this finding is emphasized by Heiberg.[11]

Summary.—It has been the purpose of this paper, in connection with the report of an instance of diabetes mellitus in early infancy, to present briefly other cases of the same disease occurring during the first year. The urinary findings are usually incomplete, but a consideration of all the symptoms given warrants the probable diagnosis of diabetes mellitus in the cases of 15 additional babies under one year reported from 1852 to the present. The majority of these cases were males.

Heredity seems to have played but little part.

Continuous over-feeding of sugar preceded the onset in three cases.

Injury to or alteration of the central nervous system was often associated with the beginning of the malady.

The more common symptoms were increased thirst and hunger, loss of weight, polyuria, and glycosuria; acidosis and coma occasionally ended the scene.

The prognosis is grave, but not hopeless, even in infancy, except in a severe grade of the disease.

Treatment should be begun early, and, although more difficult in carrying out, should follow the lines found most successful in the treatment of diabetes in adults, *i. e.*, the patient's carbo-hydrate tolerance should be determined and the sugar content of the diet (milk mixture) correspondingly reduced, the calorific requirements being furnished by fats and proteids.

An "oatmeal day" or days should be given at frequent intervals.

Diabetes mellitus is fortunately a rare affection of early infancy, but undoubtedly cases pass unrecognized, as do other conditions in babies, because of the failure to examine the urine of these patients systematically.

REFERENCES.

1. Lapine: Le Diabète Sucre, Paris, 1909, 390.
2. Kulz-Gerhardt's Handb. d. Kinderkrankh., 1878, iii, 269.
3. Stern: Arch. f. Kinderheilk., 1890, xi, 81.
4. Wegeli: Arch. f. Kinderheilk., 1895, xix, 1.
5. Von Noorden: New Aspects of Diabetes, New York, 1912.
6. Grosz: Jahrb. f. Kinderheilk., 1892, xxxiv, 83.
7. Helmholtz: Proc. Am. Ass. Study and Prevention Inf. Mortality, 1910, i, 109.
8. Aschenheim: Verhandl. d. Gesellsch. f. Kinderheilk., 1909, xxvi, 178.
9. Cobliner: Ztschr. f. Kinderheilk., 1910, i, 207.
10. Leifmann and Stern: Biochem. Ztschr., 1906, i
11. Heiberg: Arch. f. Kinderheilk., 1911, lvi, 403.

BIBLIOGRAPHY TO TABLE OF CASES.

a. Kitselle: J. f. Kinderkrankh., 1852, xviii, 313.
b. Rosbach: Berl. klin. Wchnschr., 1874, xi, 258.
c. Busch: Jahresb. ü. d. Fortschr. d. Med., 1876, cited by Stern, Arch. f. Kinderheilk., 1890, xi, 103.
d. Hagenbach: Jahrb. f. Kinderheilk., 1879, xiii, 421.
e. Garnerus: Deutsche med. Wchnschr., 1884, x, 697.
f. Nichues: Inaug. Diss. Wurzburg, 1891, cited by Wegeli, Arch. f. Kinderheilk., 1895, xix, 8.
g. Tavaria: Indian M.-Chir. Rev., 1893, i, 402.
h. Bell: Edinb. M. J., 1896, xli, 709.
i. Caillot: Cited by Baumel, Gaz. d. mal. infant., 1900, xii, 273.
k. Orloff: Vrach., March 3, 1901, Abs. Semaine méd., 1901, 192.
l. Young: Arch. Pediat., 1902, xviii, 198.
m, n, o. Langstein: Verhandl. d. Cong. f. innere Med., 1909, xxvi, 209.
p. Eaton and Woods: Tr. Am. Pediat. Soc., 1911, xxiii, 244.
r. Knox: Johns Hokins Hosp. Bull., 1913, xxiv.

THE PRODUCTION OF PASSIVE HYPERSENSITIVENESS TO TUBERCULIN.[1]

SECOND PAPER.

By CHARLES R. AUSTRIAN, M. D.,

Director of the Research Laboratory of the Phipps Dispensary for Tuberculosis; Assistant in Medicine, The Johns Hopkins University,

AND

HIRAM FRIED, M. D.,

Laboratory Assistant.

About fifteen months ago I spoke before this society on the production of passive hypersensitiveness to a tuberculo-protein; a protein since shown by work in the laboratory of the Phipps Dispensary [1] to be identical with the sensitizing fraction of tuberculin. In this report [2] the results of previous attempts passively to sensitize animals to tuberculin with the serum of tuberculous human hosts were detailed. The negative findings of Friedmann,[3] Eitner and Stoerk,[4] Roepke and Busch,[5] Novotny,[6] Onaka,[7] Simon,[8] Romer and Joseph,[9] Joseph,[10] Frankel,[11] Kraus, Lowenstein and Volk,[12] of Kraus [13] and others were mentioned. The results of Yamanouchi [14] and the evidence furnished by A. K. Krause [l.c.] discrediting them were outlined, and the doubtful character of the findings of Bauer,[15] of Helmholtz [16] and of Bail [17] were indicated. The observations of Bruck [18] alone seemed to show a measure of success in the attempts passively to sensitize normal guinea pigs with the serum of tuberculous individuals. In this preliminary report, too, the results of experiments on passive hypersensitiveness to tuberculin made in the research laboratory of the Phipps Dispensary for Tuberculosis were described and the following conclusions were drawn:

1. Tuberculin hypersensitiveness in man is a condition of true anaphylaxis and that in cases of tuberculin idiosyncracy at least sensibilisin may be present in the circulating blood; and

2. The failure of previous work may perhaps be explained on the theory that in most instances of tuberculin hypersensitiveness sensibilisin is to be found only in the tissues of the body, and either not at all, or only in minimal amounts in the circulation; whereas, in the rare cases in which a maximal grade of sensitiveness to tuberculin exists, there is sufficient circulating antibody passively to sensitize animals injected with their blood.

The work reported in this preliminary communication has been confirmed by Thiele and Embleton.[19]

The following experiments were made in order to determine if the blood or serum of tuberculous individuals, with an average degree of hypersensitiveness to tuberculin, will sensitize normal guinea pigs.

EXPERIMENTAL PART.

Thirty-five patients, all infected with the tubercle bacillus, and all showing positive von Pirquet and Calmette reactions, were studied. The technic employed was in brief as follows: Fifteen cubic centimeters of blood were obtained from each patient by vena puncture and the coagulation of the blood so drawn was inhibited by the addition of 1.5 per cent sodium citrate solution. Normal untreated guinea pigs, 250-300 grams in weight, were each injected with the equivalent of five cubic centimeters of whole blood.

Serum was used in only four experiments, inasmuch as our earlier work had clearly demonstrated that the blood is a more efficient sensitizer than is the serum. The sensitizing injections were made into the peritoneal cavities, and 20-48 hours later the guinea pigs were tested by an intracardiac injection of a solution containing 0.009-0.015 grams of tuberculo-protein prepared according to the technic of Baldwin.[20] There is no need to detail the experiments made. Briefly, it may be stated that definite positive results were obtained with the blood of only one of the patients examined.

This individual was a white man aged 32 years. He showed the signs of a moderately advanced bilateral pulmonary tuberculosis and was extremely sensitive to tuberculin. The installation of one drop of a 1 per cent solution of old tuberculin into the left conjunctival sac caused the development not only of conjunctival hyperæmia, but purulent secretion, chemosis and photophobia as well. Likewise the response to the von Pirquet skin test was very marked. The blood of this patient led in five of the six animals injected with it to the development of so sensitive a state that the reinjection of the animals with tuberculo-protein 40 hours later caused acute death. Four of the five animals that succumbed developed the typical symptoms of acute anaphylactic shock and post mortem showed the massive pulmonary emphysema, subepicardial hæmorrhages and delayed coagulation time of the blood, so characteristic of true anaphylaxis. The fifth animal showed in addition to these signs a small hæmorrhage into the pericardial sac, an accident which obscures the interpretation of the result.

It is interesting that negative results were obtained when the blood of five patients who had been treated with large doses of tuberculin was used as the sensitizing agent. This, in spite of the fact that the blood was drawn three to eight weeks after the cessation of specific therapy, at a time when *a priori* it might have been expected that active hypersensitiveness had developed, not only as a consequence of the disease,

[1] Read at a meeting of the Lænnec, a society for the study of tuberculosis, The Johns Hopkins Hospital, Apr. 28, 1913.

but from the injection of so large a quantity of foreign protein.

These experiments seem to us completely to establish the conclusions of our preliminary report already stated, and to show that free circulating sensibilisin is not present in most cases of pulmonary tuberculosis.

A valid criticism of the last statement is pertinent. The method used may not have been sufficiently refined to detect minimal amounts of the specific sensitizing substance. It may be that the blood is so diluted after injection into an animal as to provide too little of the active sensitizing agent, or that at the time it contained too little anti-substance passively to sensitize normal animals.

To overcome these objections, the blood of tuberculous patients was incubated with tuberculo-protein, with various tuberculins, or with pulverized tubercle bacilli in order to prepare anaphylotoxin according to the method of Friedberger. This procedure was adopted because it had been shown by Sata [21] that "it is possible through a simple mixing in vitro of old tuberculin or powdered tubercle bacilli with the serum of immune animals, under optimum conditions, to produce a toxin which can elicit a recognized tuberculin reaction or typical anaphylactic death in normal guinea pigs."

TABLE I (GRAY—HETROTH).

Preparation.	Incubation. Time.	Incubation. Temperature.	Weight of Guinea Pig.	Injection.	Symptoms.	Autopsy.
1.0 cc. Blood + 1.0 cc. O. T. + 0.5 cc. C.	24 hours.	37° C.	275 grams.	Intravenous 1.5 cc.	Restless.	No characteristic lesions.
1.0 " " + 0.5 " " + 0.5 " "	" "	" "	280 "	" " "	"	" " "
1.0 " " + 0.3 " " + 0.5 " "	" "	" "	260 "	" " "	"	" " "
1.0 " " + 0.25 " " + 0.5 " "	" "	" "	270 "	" " "	None.	" " "
1.0 " " + 0.2 " " + 0.5 " "	" "	" "	250 "	" " "	"	" " "
1.0 " " + 0.15 " " + 0.5 " "	" "	" "	290 "	" " "	"	" " "
1.0 " " + 0.1 " " + 0.5 " "	" "	" "	265 "	" " "	"	" " "
1.0 " " + 1.0 " Protein + 0.5 " "	" "	" "	272 "	" " "	Restless.	" " "
1.0 " " + 0.6 " " + 0.5 " "	" "	" "	265 "	" " "	Sneezing.	" " "
1.0 " " + 0.5 " " + 0.5 " "	" "	" "	250 "	Intracardiac " "	None.	" " "
1.0 " " + 0.4 " " + 0.5 " "	" "	" "	300 "	" " "	"	" " "
1.0 " " + 0.3 " " + 0.5 " "	" "	" "	280 "	" " "	"	" " "
1.0 " " + 0.2 " " + 0.5 " "	" "	" "	280 "	" " "	Death in 1 hour.	Haemorrhage into pericardial sac.
1.0 " " + 0.1 " " + 0.5 " "	" "	" "	270 "	" " "	None.	No characteristic lesions.
1.0 " " + 1.0 " Pulv. B. + 0.5 " "	" "	" "	275 "	" " "	Death in 6 hours.	Haemorrhage into pericardial sac.
1.0 " " + 0.5 " " + 0.5 " "	" "	" "	265 "	" " "	None.	No characteristic lesions.
1.0 " " + 0.3 " " + 0.5 " "	" "	" "	280 "	" " "	Immediate death.	Haemorrhage into pericardial sac.
1.0 " " + 0.2 " " + 0.5 " "	" "	" "	275 "	Intravenous " "	None.	No characteristic lesions.
1.0 " " + 0.15 " " + 0.5 " "	" "	" "	265 "	" " "	"	" " "
1.0 " " + 0.10 " " + 0.5 " "	" "	" "	290 "	" " "	"	" " "

Same scheme carried out with blood of other patients, using varying incubation periods up to 216 hours.

TABLE II (SCHAEFFER).

Preparation.	Incubation. Time.	Incubation. Temperature.	Weight of Guinea Pig.	Injection.	Symptoms.	Autopsy.
1.0 cc. Blood + 0.5 cc. Pulv. B. + 0.5 cc. C.	Immed. injec.		250 grams.	Intracardiac 1.5 cc.	Restless. Dyspneic.	No characteristic lesions.
1.0 " " + 0.5 " " + 0.5 " "	1 hour.	37° C.	250 "	" 2.0 "	" "	" " "
1.0 " " + 0.5 " " + 0.5 " "	2 hours.	" "	275 "	" 2.0 "	Sneezing. Fall of 3° C. in temp.	Haemorrhage into pericardial sac.
1.0 " " + 0.5 " " + 0.5 " "	24 "	" "	260 "	" 1.5 "	No symptoms.	No characteristic lesions.
1.0 " " + 0.5 " " + 0.5 " "	48 "	" "	255 "	" 1.75 "	" "	" " "
1.0 " " + 0.5 " " + 0.5 " "	72 "	" "	270 "	" 1.75 "	" "	" " "
1.0 " " + 0.5 " " + 0.5 " "	96 "	" "	265 "	" 1.75 "	" "	" " "
1.0 " " + 0.5 " " + 0.5 " "	120 "	" "	280 "	Postorbital 1.5 "	Immediate death.	Pontile haemorrhage.
1.0 " " + 0.5 " " + 0.5 " "	148 "	" "	270 "	" 1.5 "	Sneezing. Dyspneic.	No characteristic lesions.
1.0 " " + 0.5 " " + 0.5 " "	196 "	" "	270 "	" 1.5 "	No symptoms.	" " "
1.0 " " + 0.5 " " + 0.5 " "	216 "	" "	265 "	" 2.0 "	" "	" " "
1.0 " " + 0.5 " " + 0.5 " "	48 "	11 "	253 "	Intravenous 1.5 "	" "	" " "
1.0 " " + 0.5 " " + 0.5 " "	96 "	11 "	255 "	" 2.0 "	" "	" " "
1.0 " " + 0.5 " " + 0.5 " "	120 "	11 "	265 "	" 1.75 "	" "	" " "
1.0 " " + 0.5 " " + 0.5 " "	200 "	11 "	280 "	" 1.5 "	" "	" " "

Same scheme carried out, using varying proportions of blood and different antigens.

TABLE III (WEINBERG).

Preparation.	Incubation. Time.	Incubation. Temperature.	Weight of Guinea Pig.	Injection.	Symptoms.	Autopsy.
3.0 cc. Blood + 0.33 cc. Protein + 0.5 cc. C.[1]	24 hours.	37° C.	270 grams.	Intracardiac 1.5 cc.	No symptoms.	No characteristic lesions.
2.0 " " + 2.0 " " + 0.5 " "	" "	" "	255 "	" 1.5 "	" "	" " "
3.0 " " + 0.33 " O. T. + 0.5 " "	" "	" "	260 "	" 2.0 "	" "	" " "
2.0 " " + 2.0 " " + 0.5 " "	" "	" "	260 "	" 1.5 "	Restless. Dyspneic.	" " "
3.0 " " + 0.33 " A. F. + 0.5 " "	" "	" "	265 "	" 1.5 "	Prompt death.	Haemorrhage into pericardial sac.
2.0 " " + 2.0 " " + 0.5 " "	" "	" "	255 "	" 1.5 "	No symptoms.	No characteristic lesions.

Blood-protein mixture used in primary injections incubated up to 148 hours—negative results. C[1] = Complement (guinea-pig's serum 1-10).
O. T. = Old tuberculin. A. F. = Albumose-free tuberculin. Pulv. = Powdered tubercle bacilli. Protein = Protein obtained by aqueous extraction of tubercle bacilli.

The details of the technical procedures will not be considered here. The serum and the citrated blood of the tuberculous hosts were incubated for varying periods of time (3-16 hours) and at different temperatures (6 to 40 degrees centigrade), with old tuberculin, albumose-free tuberculin, pulverized tubercle bacilli and so-called tuberculo-protein, in proportions that varied from one to one to nine to one. At the end of the incubation period the serum or the blood protein mixtures were centrifugalized and the supernatant fluid

was injected into normal guinea pigs. The test solutions were introduced into the heart, the jugular vein or the subdural space of the animals. Not only were manifest symptoms of hypersensitiveness watched for, but variations of temperature were noted. The tables clearly illustrate the procedures employed in some of the many experiments made.

For the sake of brevity suffice it to state that though the blood and the serum of patients were tested by this method; that though many combinations of varying quantities of blood or serum with complement and antigen, and variations of the duration and the temperature of incubation were tried, no definite positive results were obtained. Some of the animals tested did develop symptoms, but the nature of them was equivocal; some of them did show marked variations in temperature, sudden rises or falls, but in no instance did acute lethal shock develop.

These results confirm the established fact that free sensibilisin, at least with the methods employed, is not to be demonstrated in the circulation of most individuals with pulmonary tuberculosis. However, the positive findings recorded in our preliminary paper and in the experiments just described, though exceptional, are important as evidence in establishing the anaphylactic nature of the tuberculin reaction.

BIBLIOGRAPHY.

1. C. R. Austrian: Johns Hopkins Hosp. Bull., 1913, xxiv, 141.
2. C. R. Austrian: J. Exp. Med., 1912, xv, 149.
3. U. Friedman: München. med. Wchnschr., 1907, liv, 2414.
4. E. Eitner and E. Stoerk: Wien. klin. Wchnschr., 1909, xxii, 808.
5. Roepke and Busch: Beitr. z. klin. d. Tuberk., 1909, xiv, 147.
6. J. Novotny: Ztschr. f. Immunitätsforsch., 1909, ii, 679.
7. M. Onaka: Ztschr. f. Immunitätsforsch., 1910, v, 264; 1910, vii, 507.
8. S. Simon: Ztschr. f. Immunitätsforsch., 1909-10, iv, 547.
9. P. H. Römer and K. Joseph: Berl. klin. Wchnschr., 1909, xlvi, 1300.
10. K. Joseph: Ztschr. f. Immunitätsforsch., 1910, iv, 575.
11. E. Frankel: Centralbl. f. Bakteriol., Orig., 1911, lviii, 460.
12. R. Kraus, E. Lowenstein and R. Volk: Deutsche med. Wchnschr., 1911, xxxvii, 389.
13. A. K. Krause: J. Med. Res., 1910, xxii, 257.
14. T. Yamanouchi: Wien. klin. Wchnschr., 1908, xxi, 1623.
15. J. Bauer: Müchen. med. Wchnschr., 1909, lvi, 1218; Beitr. z. klin. d. Tuberk., 1909, xiii, 383.
16. H. F. Helmholz: Ztschr. f. Immunitätsforsch., 1909, iii, 371.
17. O. Bail: Ztschr. f. Immunitätsforsch., 1909-10, iv, 470.
18. C. Bruck: Berl. klin. Wchnschr., 1910, xlvii, 517.
19. F. H. Thiele and D. Embleton: Ztschr. f. Immunitätsforsch., 1913, xvi, 411.
20. E. R. Baldwin: J. Med. Res., 1910, xvii, 189.
21. A. Sata: Ztschr. f. Immunitätsforsch., 1913, xvii, 84.

SOME STRIKING EXAMPLES OF SUBNORMAL ACCOMMODATIVE POWER.[1]

By Samuel Theobald, M. D.,

Clinical Professor of Ophthalmology, The Johns Hopkins University.

Twenty-two years ago, in a paper read before this society, and published in the Transactions for 1891,[2] I first described the condition for which the name "subnormal accommodative power" was suggested—a condition which I then believed to be, and now, with more extended experience, know to be, "a not infrequent cause of asthenopia in young persons." Three years later, in a shorter communication to this society,[3] I reported several typical cases of this condition, and mentioned, as bearing upon the relative frequency of its occurrence, that in 1615 consecutive cases of refractive and muscular anomalies met with in private practice which I had then recently tabulated the presence of subnormal accommodative power, more or less marked, was noted 155 times—about 9.50 per cent of the whole number of cases. More recently I have gone over the notes of 200 cases, many of them being those of persons beyond the presbyopic age, in whom the condition can seldom be recognized; included under the letters A and B in a later series of refractive and muscular faults, and found 22 cases of subnormal accommodative power—a little over 10 per cent of the total.

As my views regarding the nature of this anomaly and the means of detecting and dealing with it were fully set forth in the first paper upon the subject, to which I have referred, and more recently in my treatise upon "Prevalent Diseases of the Eye," I shall not lengthen this communication by repeating much that has already been said, but will content myself with the statement that the doctrine of subnormal accommodative power is based upon the observation that, while the normal balance of the lateral muscles of the eyes in distant vision, as shown by the vertical diplopia test, is one of orthophoria, in *near* vision (at the usual reading distance), the normal condition, as shown by the same test, is one of exophoria, there being usually a relative divergence of 3° to 4°. In other words, with induced vertical diplopia, exophoria of moderate degree at the reading distance is the real orthophoric condition, while "orthophoria," using the term as it is commonly employed, when present in near vision (with vertical diplopia) is a departure from the normal, and is to be regarded as truly a heterophoric condition. Expressed in another form, the vertical diplopia test at the reading distance should show, as compared with the result at 20′, a difference in the sense of exophoria of 3° to 4°. When this is not the case subnormal accommodative power exists, and if the difference is 0° or but 1° it must be taken into account in the

[1] A paper read before the American Ophthalmological Society, Washington, May 7, 1913.

[2] Vol. VI, p. 127.

[3] Vol. VII, p. 138.

adjustment of glasses, if the patient is to obtain comfortable near vision.

In this connection it may be of interest to mention that Mr. F. W. Weymouth, a graduate of Leland Stanford University, who during the past winter has been engaged in post-graduate work, under Prof. W. H. Howell, in the physiological laboratory of The Johns Hopkins University, has recently made a study of the muscle balance, the range of accommodation, etc., of the eyes of 40 students in The Johns Hopkins Medical School. His carefully-conducted measurements showed for the whole number of eyes tested an average esophoria, in distant vision, of a small fraction of a prism-diopter, whereas in near vision, at 32 cm., he found an average exophoria of 5.02 prism-diopters, a difference, in striking confirmation of the view commonly held by ophthalmologists, of slightly more than 5 prism-diopters.

A goodly number of my ophthalmological confrères have been sufficiently impressed by the views I have advanced regarding the significance of subnormal accommodative power to put them into practice, and from some of them I have received gratifying reports as to the satisfactory results which they have obtained from doing so; but, judging from my clinical experience, a considerably larger number, it would seem, have not been so impressed; and, taking a narrow view of the matter, perhaps I should not complain of this, since it has afforded me not a few opportunities to relieve troublesome cases of asthenopia, when their efforts have been without avail.

I might cite a large number of cases in which the prescribing of glasses for subnormal accommodative power has proved most helpful; but it has seemed to me that a brief description of a few typical and striking examples of this anomaly would be more to the purpose.

CASE I.—Mr. H., æt. 42, engaged in newspaper editorial work in Philadelphia, and, therefore, compelled to use his eyes a great deal, especially at night, consulted me in January of this year. His asthenopic symptoms were very pronounced and he feared he would have to abandon his profession. He had not long before consulted an eminent ophthalmologist in his own city, who had given him glasses for near vision which corrected a low degree of astigmatism, and slightly over-corrected his manifest hypermetropia, from which, however, he derived but little relief.

With lenses which fully corrected his manifest fault and gave him $\frac{20}{XV}$ vision, I found his muscle balance at 20′, by the vertical diplopia test, varied from slight exophoria to orthophoria; but, when the test was repeated at the reading distance, 13″, marked esophoria was revealed, which, even with the addition of +.62s to the distance correction, amounted to 4½°. When + 1.37s, instead of +. 62s, was added to the distance lenses his near muscle balance varied from "orthophoria" (so-called) to esophoria of ½°, and, in reading, he willingly accepted, in addition, 3° of esophoric correction.

For distant vision lenses were prescribed as follows:

L. eye +.37s = +.37c 130°.
R. eye + .75s = —.50c 95°.

And for near vision:

L. eye + 1.75s = +.37c 130° = prism 1½° base out.
R. eye + 2.12s = —.50c 95° = prism 1½° base out.

Although he has not worn the distance lenses systematically, as advised, his asthenopia has been completely relieved by the near glasses, and up to the present time he has been able to continue his editorial work with comfort.

It would be difficult to find a more typical example of subnormal accommodative power than is afforded by this case, or a better illustration of the benefit which results from its recognition and correction. Probably because of congenital insufficiency of the ciliary muscles, an inordinate accommodative effort was required to maintain distinct near vision; but, because of the close relation between the accommodative and convergence centers, a strong stimulation of the ciliary muscles was necessarily accompanied by a corresponding stimulation of the internal recti; hence the esophoria, present only in near vision, and hence also the asthenopia, which commonly manifests itself, as is generally recognized, when the normal parallelism between convergence and accommodation is radically disturbed. The glasses prescribed, which afforded a considerably greater measure of help to the ciliary muscles than the refractive fault or the age of the patient called for, while at the same time they appreciably lessened the tension upon the hard-pressed external recti, relieved the asthenopia by restoring this normal parallelism.

It is interesting to note that two children of this patient, aged, respectively, 9 and 7 years, exhibit, to a less degree, the same fault as the father, for which both are wearing glasses.

CASE II.—Mr. A., æt. 26, a medical student in Johns Hopkins University, although his hypermetropic astigmatism had been accurately corrected by a confrère, still complained of asthenopia in near vision. In explanation of this he was found to have well-marked subnormal accommodative power. The glasses finally decided upon for distance were:

L. eye +.62c 160°.
R. eye +.50c 15°.

With these he had, for the two eyes, $\frac{20}{XV}$ + vision, and at 20′ an esophoria of 1°, but at 12″ an esophoria of 3½° was found. The addition of + 1.s to the distance correction sufficed only to eliminate this esophoria, and, theoretically, he should have had a stronger spherical lens than this, or some esophoric prismatic help, for near vision. It was decided, however, to try the effect of adding + 1.s to the distance lenses, and this proved entirely successful; and to the present time he has been using these glasses in near vision and doing much hard work with his eyes without discomfort.

CASE III.—Mr. B., æt. 23, a student in The Johns Hopkins Medical School, with decided asthenopia and occasional diplopia in near vision, had consulted a well-known oculist in Washington, who prescribed for near vision:

L. eye — .25c 180°.
R. eye — .12s = — .50c 170°

As these failed to relieve the asthenopia, he subsequently came to me. Upon testing his muscle balance he was found to have, with these glasses, an esophoria at the reading distance of 5°; without glasses, an esophoria at 20′ of 1°, scant, was found — definite proof of subnormal accommodative power. He was given for near use:

L. eye +.87s.
R. eye +.50s = +.37c 75°.

With these he showed an exophoria at 12″ which varied from 1° to 0°. His asthenopia promptly disappeared. Some months later there was a return of the symptoms, when a change in the astigmatic correction, but not in the spherical, was found to be necessary.

Case IV.—Miss D., æt. 19, was asthenopic and suffered with severe headaches. She was found to have a low degree of compound myopic astigmatism, complicated by pronounced subnormal accommodative power. For distance, glasses were ordered as follows:

L. eye $-.37s = -.25c\ 50°$.
R. eye $-.12s = -.25c\ 90°$.

With these she had $V = \frac{20}{XV}$ —and orthophoria at 20′; but at 12″ an esophoria varying in degree, at times amounting to 6°, was revealed. With + 1.25s added to the distance correction there was still no exophoria at the reading distance. For near vision,

L. eye $+.87s = -.25c\ 50° =$ prism 1° base out
R. eye $+1.12s = -.25c\ 90° =$ prism 1° base out

were prescribed, and as she was not heard from again it is fair to presume that they afforded the desired relief.

It may be mentioned, as of interest, that this patient had been in the habit of holding a book, in reading, very close to the eyes, as though she were highly myopic, a circumstance not very unusual in high degrees of subnormal accommodative power. The explanation of this paradox evidently is that the individual finds the greater accommodative effort required in doing this more than offset by the greater compensating convergence which attends it. When the proper convex glasses are given the habit promptly disappears and the book is held at a normal distance.

It seems unnecessary to lengthen this paper with further reports of cases, for those which I have briefly described suffice to make clear the signficance of the anomaly, the tests depended upon to reveal its existence, the annoying asthenopic symptoms to which it gives rise, the measures demanded for its correction, and the immense relief which these measures invariably afford; and this was all I had in view in bringing the subject once more to the attention of the members of the Ophthalmological Society.

UNILATERAL SCLEROSIS OF THE PULMONARY ARTERY.

By Frank A. Evans.

(From the Pathological Laboratories, University of Pittsburgh, Pittsburgh, Pa.)

These studies were undertaken upon the presentation of a particularly interesting case, which showed an advanced unilateral sclerosis of the pulmonary artery associated with a condition of collapse and fibrosis of the opposite lung. This remarkable association, with such a striking difference in the character of the vessels of the two lungs, offered an excellent opportunity to investigate the pathological process which had occurred in the arteries and to associate these changes with the altered conditions in the pulmonary circulation.

It is rather infrequent in the human subject to have an opportunity of studying semi-experimental circulatory disturbances having pathological changes in the arteries as their sequel. Here, however, in a paired organ there was demonstrated a process by which the circulation had been profoundly altered in the one and which had secondarily led to circulatory changes (it may be increased pressure) in the arterial tree of its fellow organ.

The presence of small isolated nodules upon the surface of the pulmonary arteries has been repeatedly commented upon and these lesions are not uncommonly found, when properly searched for, in individuals above middle age. These nodular elevations, which present a yellow appearance, are seen at the points of bifurcation of the pulmonary arteries, as well as along the main stem. There appears to be no difference in their distribution in the two lungs, nor does it appear that any one lobe is affected more than another. These small plaques in the pulmonary vessels seem to bear no relation to changes occurring in the systemic arteries. At times, however, these sporadically distributed nodules are more extensive, showing actually atheroma and calcification, and, as in the case of Ruppert, leading to a narrowing in some of the branches. Somewhat similar cases are reported by White, Kidd, McPhedran, and Mackenzie. On the other hand, Thorel believes that the pulmonary scleroses differ essentially from those occurring in the aorta and that they are rather of a character of medial sclerosis due to calcium metastasis. Several cases have been described in which this condition of medial degeneration with but little intimal sclerosis has been the main finding.

It would appear, however, that as the arteries of the lesser circulation differ in no essential way from the systemic vessels and the influences brought to bear upon them are, in many respects, similar, the lesions occurring in them are comparable. This view is taken by Torhorst and Ehlers. To these we will refer again.

We have undertaken the histological examination of the pulmonary arteries of the case in question and have further compared the lesions observed in it with the nodular variety which is more commonly encountered in elderly persons.

Before entering upon the essential points in these pathological processes it is necessary to briefly indicate the histology of the pulmonary artery. The structure of these vessels we have found to compare closely with the description given by Torhorst, and his anatomical arrangements will be used as the basis upon which the arteriosclerotic changes are discussed in this paper.

The normal structure of the pulmonary artery and its main branches simulates very closely the architecture of the aorta. The outermost coat is represented by an adventitia consisting of a loosely arranged fibrous tissue interspersed by some elastic

fibers and having occasional longitudinal bundles of muscle fibers scattered through it. Nutrient vessels of different sizes course through its loose connective tissue. Closely applied to its inner border is the media characterized by many strong elastic fibers, circularly disposed, and between them are muscle cells set at all angles, but principally having a circular direction. Along the inner border of this laminated coat is the musculo-elastic layer running longitudinally to the vessel, but whose individual muscle bundles crossing each other at acute angles form a net work. This musculo-elastic layer also contains elastic fibers, which along its inner border are aggregated into a denser bundle to form the inner boundary between this layer and the intima proper. The intima which is the innermost layer has, in the main, a circular direction and is made up of connective tissue, but is rich in fine elastic fibrils often giving the appearance of strong elastic tissue fibers. In the small arteries both the musculo-elastic and connective tissue layers are thin and weak.

Although our study deals more particularly with the changes in the pulmonary artery, we have added some of the history as well as a detailed description of the lungs, so that the points bearing upon the etiology of the pathological processes may be appreciated.

Mrs. X, age 39. The patient's family and previous history were negative. She claimed to have been well until a year ago. She was married and had nine children, three of whom died in infancy. She had one miscarriage of twins seven months old, just before the onset of her present illness, and has not menstruated since. She has always worked hard and her habits of life have been good; she denied lues.

Her present illness began with the miscarriage, for upon getting up after this confinement, December 25, 1909, she noticed her feet and ankles were swollen. This condition progressed and in three days her feet and legs were excessively swollen as far as the knees, so that she thought they would burst. Then the abdomen began to swell and at the end of a week "was filled as tight as a drum." She then went to a hospital, where she remained for five weeks, with no benefit, except that the swelling of her feet and ankles somewhat subsided. This œdema returned as soon as she got up, and she again returned to the hospital for two weeks, and later again for six weeks, but did not improve. Since June 3, 1910, she has been at home. Ever since the miscarriage she has been cyanotic, especially about the face, and worse when she was on her feet. About three months previous to exitus she began to be troubled with pain and soreness in the liver region and entered the Mercy Hospital. These symptoms were severe and for the last three weeks of her life she suffered continuously. No history was obtained of a previous acute intrathoracic lesion.

Autopsy.—No. 60, November 27, 1910. Dr. S. R. Haythorn.

The body was that of a well-developed woman, 146 cm. tall. The tissues of the face, ears, lips and extremities had a purplish-blue appearance as of venous congestion. The scleræ were slightly jaundiced. Large distended veins were present over the lower portion of the abdomen, as well as on the lower extremities. There was an œdema of the lower abdomen and extremities.

In the thorax extensive adhesions were found in the right pleural cavity, almost completely obliterating it. The right lung was very small and was crowded towards the vertebral border, and was firmly held in this position by the adhesions. The left pleura was free and the lung appeared of more than normal size. The pericardium contained over 300 cc. of a clear fluid.

Heart: Weight 385 gm. Over the right auricle and ventricle were several milk spots, the largest being 1.5 cm. in diameter. The right auricle was much dilated, and the right auricular appendix contained a laminated red and gray clot. The coronary sinus appeared to be dilated at its mouth. The cavity of the right ventricle was large and the muscular wall appeared quite thick (12 mm.). The papillary muscles in the right ventricle looked like those of the left heart. The whole structure of the right heart was hypertrophied. The tricuspid and pulmonary valves were all thin and leaf-like, showing no evidence of sclerosis. The base of the pulmonary artery showed some diffuse and nodular thickening of the intima, with some areas showing deep fatty change. The left heart was well contracted and the cavities were empty. Both auricle and ventricle appeared of the usual size and showed no definite change. The mitral valve was a little grayish and slightly thickened. The aortic leaflets appeared healthy. The base of the aorta showed a few small nodules of sclerosis close to the openings of the coronary arteries. The coronary arteries showed no evidence of sclerosis. The foramen ovale was patent. The arteries

FIG. 1.—Left lung, showing marked sclerosis of pulmonary arteries.

of the systemic system showed only occasional and slight sclerosis at the points of bifurcation.

Left Lung: The organ was diffusely enlarged and appeared overdistended. It was free from adhesions and the outer surface was marbled by a considerable deposit of coal pigment. Over the pleura were a considerable number of white and well-defined lines following the course of the lymphatic channels. The organ crepitated throughout. There was no evidence of consolidation or of tuberculosis. The cut surface of the lung presented a very remarkable appearance, in that the blood vessels in both lobes stood out very prominently, giving them, at first sight, the appearance of bronchi. The main trunk of the left pulmonary artery was irregularly thickened and the intima was quite nodular. The thickening, though nodular, was diffuse and affected the circumference of each vessel. Many of the vessels were of cartilaginous hardness. In places the lumen of the artery was distinctly narrowed, while in other places small pouches occurred in the course of the vessel and particularly at the points close to a bifurcation.

Right Lung: The surface of the organ was covered by extensive old adhesions. The organ was very small and collapsed and formed a little shrunken mass lying in the upper and inner part of the chest cavity. This lung was meaty in character, and contained but little air. The tissues were, in part, firm and somewhat fibrosed. There was no evidence of tuberculosis. The bronchi were small and quite pale. The pulmonary arteries were thin-walled and no evidence of sclerosis could be observed in any of them. The lung on section showed no evidence of consolidation, but the lung tissue was tough and almost airless. There was a fair amount of anthracotic marbling through this organ.

In the remaining parts of the body no important findings were made other than the presence of a considerable ascites and a congestion of the veins in the abdomen and extremities. No evidence of any chronic infective process or of syphilis was obtained.

The microscopical examination of the right lung showed a condition of collapse of the alveoli, with a thickening of the alveolar walls. The lining cells of the air sacs were prominent and frequently were of a cuboidal nature. A considerable number of desquamated cells were present within the alveoli. Besides a general thickening of the alveolar walls, small patches of fibrosis were found scattered through the lung tissue. The vessels showed a fair amount of carbon pigment surrounding them, but their walls were unchanged. There was no evidence of old or recent inflammatory reaction within the essential tissues of the arteries, although some of them showed fibrosis of the stroma in which they rested. Here and there this fibrous tissue contained small collections of lymphocytes. Nodular endarteritis was entirely lacking in the vessels of this lung.

In the left lung the alveoli were large and distended. They were, in the main, free from exudate, save some small collections of leucocytes close to some small bronchi. The alveolar walls were quite thin. The striking feature throughout the structure of this lung was the extensive and irregular nodular thickening of the arteries. This thickening was not accompanied by any change in the lung tissue immediately surrounding the arteries, although the large vessels were accompanied by a fair amount of fibrous tissue and anthracosis. The thickening was confined to a reaction in the intima, the media and adventitia remaining undisturbed as far as the microscopical examination could determine.

The remarkable unilateral sclerosis of the pulmonary artery associated with collapse and fibrosis of the lung on the opposite side, as well as with a decided hypertrophy of the right heart, led us to study more minutely the changes in the pulmonary arteries. As has been above described, the thickening of the pulmonary arteries was diffuse and nodular, and macroscopically it appeared that the nodular change was only a more intense and localized condition of the diffuse intimal sclerosis. Portions of the pulmonary artery were selected from different areas in the left lung so that the histological characters of the sclerosis might be studied in all its phases.

Microscopical Examination of Pulmonary Artery.

Main Branches: The microscopical examination of the pulmonary arteries immediately revealed the fact that an important change had occurred in the intima. In the areas where the thickening was of a diffuse nature the media and adventitia were quite loose and devoid of any evidence of inflammatory infiltration. The nutrient vessels were not increased in number, but many of them showed some narrowing of their lumen. The outer two-thirds of the media was regularly disposed with alternating layers of elastic fibers and muscle cells. On the other hand, the inner layer of the media was somewhat changed through the loss of muscle fibers and the more close packing together of the elastic strands. In this situation the areas previously occupied by the muscle cells now showed the presence of granules of a fatty nature. Thus with the sudan stain a narrow layer of fatty degeneration affecting the muscle fibers of the innermost zone of the media was easily demonstrated, and the reaction and degeneration were more evident here than in the diffusely-thickened tissues of the intima. This, however, was not the case where the intima showed nodular thickening, in which the extensive degenerations were found in the deep portion of the intima.

The internal elastic lamina was, for the most part, broken up into a multitude of fine fibrils. Intermingled with these elastic fibers was a varying amount of muscle tissue having a longitudinal direction. For the most part, there was some increase in the quantity of the muscle tissue in this layer. More or less fatty degeneration was also present in these muscle cells, but where the intima was only moderately and diffusely thickened the amount of fatty change was not great.

The diffuse thickening of the intima proper was mainly the result of a hyperplasia of the connective tissues and elastic fibrils lying between the endothelium and musculo-elastic layer. Nevertheless, occasional strands or small bundles of muscle tissue were found to extend into this layer from the deeper musculo-elastic lamina. The connective tissue thickening consisted of a compact layer in which the connective tissue cells were longitudinally disposed, and, in places, were quite regularly arranged in layers. In other places, again, this connective tissue appeared looser and the cells had a more stellate appearance. The matrix in which the connective tissue cells rested was hyaline in appearance, which sometimes took on an œdematous character.

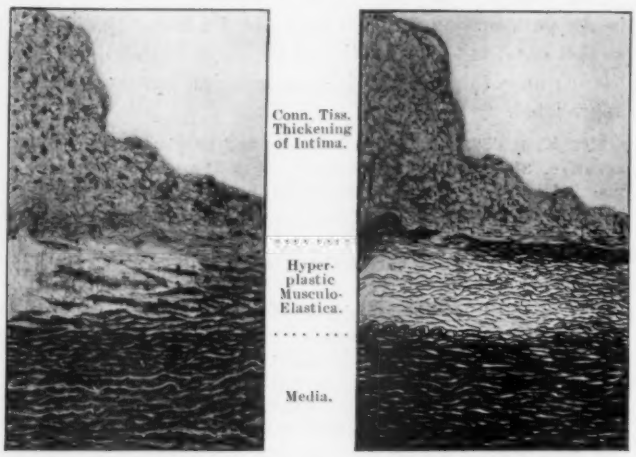


Fig. 2.—Sclerosis of pulmonary artery, showing hypertrophy of musculo-elastic layer and hyperplasia of connective-tissue layer of intima.

The nodular thickening of the arteries was a process lying entirely on the inner side of the internal elastic lamina, in which a reaction of both proliferation and degeneration was evident. The proliferative change consisted chiefly in a thickening of the connective tissue beneath the endothelium, in which relatively few elastic fibers were to be found. This hyperplasia was made up of spindle-shaped cells which were arranged more or less loosely and in a parallel manner. Where the tissue was less compact the cells had stellate characters. Near the surface this newly developed connective tissue was well retained and showed no evidence of degeneration. Close, however, to the boundary between intima and

media, extensive fatty change involved the various elements including the muscle and elastic fibers of the immediate vicinity. This process of degeneration was not alone to be observed in the intima, but extended into the media for a short distance. Thus in the vicinity of the musculo-elastic layer no definite structure could be made out, but there atheroma was involving the several tissues. For the most part these nodular areas were similar, but it was observed that some of them gave distinct evidence of inflammatory cells, mainly lymphocytes, scattered through them. It was also observed that the adventitia opposite these nodular areas showed some slight inflammatory reaction in the vicinity of the vasa vasorum. Furthermore, where the nodular thickening of the intima was extensive, the media was thinner than in the remaining portion of the vessel wall.

Small Branches: In examining the lung tissue, extensively sclerosed arteries and arterioles of small size are encountered. In fact, throughout the lung tissue, wherever small arteries are met with, sclerosis of their structure is found. This sclerosis simulates in every respect the changes observed in the larger arteries. The

FIG. 3.—Sclerosis of branch of pulmonary artery, showing intimal thickening with deep fatty degeneration.

lesion is for the most part confined to the intima and is of proportionately greater extent than in the large vessels. The lumen is greatly reduced and the architecture of the internal layer much altered. The adventitia and media show relatively little change save that here and there a slight amount of inflammatory infiltration can be seen near the nutrient vessels. On the other hand, the internal elastic lamina and all that lies within it are much altered. The internal elastic lamina commonly shows a splitting into multiple layers, but there is no evidence of any extensive formation of elastic fibrils on the tissue of the greatly thickened intima. There is a thick layer of connective tissue between the musculo-elastic layer and the lumen. The amount of this connective tissue varies in each vessel, as well as on different sides of the same artery. In every instance much atheroma is found in the deep portion of the newly formed tissue, and this fatty change of the intima has also extended into a portion of the media. Inflammatory cells, mainly of the nature of lymphocytes, associated with a few polymorphonuclear leucocytes and plasma cells, are also seen. The musculo-elastic layer shows an irregular amount of hypertrophy, as well as evidence of degeneration. The hypertrophy of this layer does, however, not make up for much of the wide spread thickening observed throughout the arteries. This hypertrophy of the musculo-elastic layer is not uniform and, in places, is wanting.

Arteries of Right Lung: Sections made of the various arteries in this organ showed a normal structure to be present in all of them. Only very occasionally in some of the large branches were some microscopic evidences of an increase in the connective tissue layer of the intima observed. The media and the adventitia appeared normal, there being no evidence of inflammation or sclerosis. No evidence of degeneration was evident in any portion of the pulmonary artery of the right lung.

To resume, the case was one of a woman, aged 39, who died with symptoms of failure of the right heart, with chronic passive congestion, ascites and œdema, in less than a year after a twin pregnancy, which ended in a miscarriage at the seventh month. In addition to the clinical findings, the autopsy revealed a hypertrophied right ventricle and a completely collapsed right lung with firm old pleural adhesions rendering

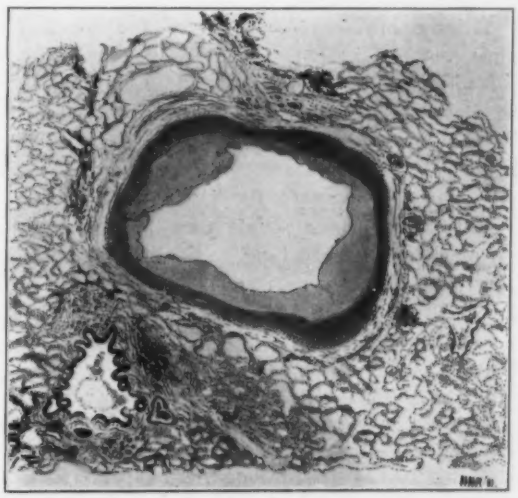


FIG. 4.—Sclerosis of small branch of pulmonary artery.

this lung almost, if not completely, incapable of functioning. The left lung showed some compensatory emphysema and an arteriosclerosis of the pulmonary arteries, which was distributed throughout both lobes. The extensive arteriosclerosis began at the left pulmonary artery and was distributed as a diffuse and nodular disease throughout its branches. The disease was one of the intima in which hypertrophy of the musculo-elastic layer was commonly found, while an extensive connective tissue proliferation underneath the endothelium had led to much irregular distortion and narrowing of the lumen. The hypertrophy in these tissues was followed by a considerable fatty degeneration which involved the tissues of the intima and sometimes attacked the neighboring media. The elastic tissue showed little evidence of proliferation, but the internal elastic lamina was broken up into multiple strands. The narrowing of the lumen was in some instances very extensive, and simulated the sclerotic condition of the arteries of the systemic

tree, showing endarteritis chronica deformans. Not uncommonly the process of hypertrophy of the musculo-elastic layer, hyperplasia of the sub-endothelial connective tissue and extensive fatty degeneration were to be observed in the same specimen. None of the vessels showed lesions which simulated syphilis.

In view of the absence of syphilis in any part of the body, as well as evidence of any definite infective process to which the unilateral arteriosclerosis could be ascribed, the actual condition found in the respiratory system is worthy of close consideration. We have evidence in the hypertrophy of the right heart of an increase in the resistance of the blood flow through the lesser circulation and in explanation of this we have the presence of an almost completely collapsed right lung of some time standing. The presence of fibrosis within this organ, as well as the firm bands of connective tissue which bound it down, were instrumental in impeding the blood flow through this lung. It is interesting to note that with the diminishing circulation in this organ no reaction of the nature of compensatory hypertrophy of the intima of the pulmonary arteries of the right side, as would be expected from the theory of Thoma, was found. Here we had every condition making for a slowing of the blood stream and for a disproportion between the blood content and the vessels' walls, and yet no definite organic change developed. On the other hand, the left lung responded in a compensatory emphysema to the respiratory incompetence of the organ on the right side. Moreover, the pulmonary circulation was very much disturbed by the collapse of the right lung, so that a greater amount of blood was required to pass through this one organ. It is probable, although this is not entirely proved in this case, that the blood pressure in the right pulmonary circulation was increased. The hypertrophy of the right heart is an evidence of this. This increased blood pressure was mainly borne by the vessels of the lung, which was functioning in an excessive degree.

For comparison we have examined five other cases in which minor scleroses, usually of the nature of isolated plaques, were found irregularly scattered through the main arteries. In two of the cases the arterial changes consisted of a connective tissue thickening of the superficial intima without showing any evidence of proliferation in the musculo-elastic layer, or any sign of degeneration. The findings in these vessels appeared to be only incidental to the cause of death and the post mortem findings. In the three other cases not only was a connective tissue proliferation observed along the inner border of the intima, but in each there was found an hypertrophy of musculo-elastic layer, with more or less evidence of degeneration in this tissue. These latter cases were associated respectively with (1) heart, kidney, and arterial disease, (2) recurrent heart disease, and (3) chronic heart disease with gonorrhoeal polyarthritis. It would appear that, when circulatory disturbances are such that an alteration in the blood pressure of the pulmonary system is brought about, an hypertrophy of the musculo-elastic layer is an early response to this change. On the other hand, nodular thickenings may also occur in the pulmonary system simulating the chronic endarteritis of Virchow. It would thus appear that the pulmonary arteries respond in a manner quite similar to the arteries of the systemic circulation.

Both Torhorst and Ehlers concluded that degenerative changes in the pulmonary artery begin in the musculo-elastic layer, simulating the reaction which Jores described for the aorta. Just as Jores indicated the development of two different types of reaction, the "hyperplastic intimal thickening," involving the musculo-elastic layer and the inner elastic lamella, and the "regenerative connective tissue increase of the intima," originating in the innermost layer, so have all investigators of the scleroses of the pulmonary arteries described reactions of a like kind. Ehlers' studies on pulmonary arteriosclerosis led him to conclusions in agreement with those of Jores, namely, that the connective tissue thickening of the intima commonly followed upon a primary degeneration of this hyperplastic musculo-elastic layer. This, on the other hand, Torhorst did not find, but he believed that the connective tissue thickening of the intima which brings with it a rich supply of fine elastic tissue was primary and together with the hyperplasia of the musculo-elastic layer formed the reaction in response to the increase in blood pressure. These two types of reaction, or according to some, these two stages of the same reaction, which resemble very much those reactions of the aorta named by Jores, "hyperplastic intimal thickening," and "connective tissue increase of the intima," are processes which take place in two different layers, normally seen in the large arteries of the lesser circulation. The first type, which corresponds to the "hyperplastic intimal thickening," consists of an hypertrophy of the musculo-elastic layer, or the "longitudinal layer" of Ehlers, with a change in the internal elastic lamella. The muscular elements increase and the elastic tissue becomes more abundant, and by the crowding together of the elastic tissue fibrils the appearance of newly developed strong fibers becomes marked. This may occur without any involvement of the internal elastic lamina, but usually the hypertrophy of the muscular elements results in a splitting of the strong elastic fibers, with the result that more fine ones come to view, giving the appearance of an equal amount of elastic tissue, spread over a greater area. The second type of sclerosis, which corresponds to the "connective tissue increase of the intima," consists of an increase of the innermost connective tissue layer of the intima. This layer may become thicker as a result of the proliferation of sub-endothelial connective tissue and may or may not be rich in fine elastic tissue fibrils. The connective tissue may increase out of proportion to the elastic tissue and result in a considerable intimal thickening, comparatively poor in elastic tissue fibrils, or even free from them along the inner edge. On the other hand, the elastic tissue of the innermost layer may increase to an unusual extent, resulting in the crowding together of the fine fibrils and giving the appearance of stronger ones in a comparatively thin margin of tissue. Fatty degeneration, though undoubtedly starting in the musculo-elastic layer and probably in the muscle cells or the new formed connective tissue, may spread both inward and outward and involve both intima and media. Later the intima

may show a type of hyaline degeneration and this without much thickening.

In view of these observations the question arises whether one can definitely determine whether the thickening of the innermost layer of connective and elastic tissue or the hypertrophy of the musculo-elastic layer was primary to the degeneration, as observed in our case of blood pressure sclerosis of the pulmonary arteries. The microscopical study showed both types of change to be present, the hypertrophy of the musculo-elastica, with splitting of the fibers of the internal elastic lamina, being the most striking. However, in most of the areas of degeneration there was a great excess of connective tissue in the overlying layer, and it was shown that the nodular eminences observed macroscopically were due to this thickening of the innermost layer.

To sum up, all the cases studied showed plaques on the pulmonary arteries having a gross appearance more or less resembling each other, but differing slightly in color and extent of distribution. In our first case were observed conditions which indicated increased blood pressure as a possible etiological factor, but in all the others no definite etiology could be assigned, and they are probably examples of the common types of arteriosclerosis of the pulmonary arteries, associated with some general arterial or other changes as a result of systemic processes. In both the former and the latter the type seen in the pulmonary arteries was comparable to the "hyperplastic intimal thickening," and of the type related to the "regenerative connective tissue increase of the intima," as described by Jores for the aorta.

As the intimal changes in our principal case were so advanced, it is impossible to say which of the proliferative reactions was primary. In none of the vessels was a pure form of proliferation of either the superficial or deep intimal layer to be found. It was, however, evident that the process of degeneration began in the hypertrophied musculo-elastic layer and from here extended into the connective tissue thickening, as well as into the media. Nevertheless, it is quite possible that the presence of the deep degeneration in the intima acted as a stimulus calling forth a still further proliferation in the overlying connective tissue. We believe, however, that, like the reaction in the systemic arteries, the hypertrophy of the musculo-elastic layer was the result of the abnormal circulation in the one lung following upon an impeded circulation on the opposite side. The process of degeneration was secondary to the proliferative reaction.

In conclusion, I wish to express my appreciation of the privileges I have enjoyed at the Pathological Laboratory of the University of Pittsburgh, and to thank Dr. Oskar Klotz for the many courtesies I have received.

BIBLIOGRAPHY.

Ehlers: Virchow's Archiv, 1904, CLXXVIII, 3.
Jores: Arteriosclerose, Wiesbaden, 1903.
Kidd: Tr. Clin. Soc. London, 1903, XXXVI.
Ruppert: Ziegler's Beiträge, 1905, VII. Suppl.
Thoma: Virchow's Archiv, 1886, CIV, 421.
Thorel: Lubarsch-Ostertag Ergebnisse, 1907, Abt. 11, 519.
Torhorst: Ziegler's Beiträge, 1904, XXXVI, 2.
Virchow: Virchow's Archiv, 1879, LXXVII, 380.

THE VALUE OF NASO-PHARYNGEAL SURGERY IN THE TREATMENT OF CHRONIC EXUDATIVE OTITIS MEDIA.[1]

By H. O. REIK, M. D., Baltimore, Md.

That chronic exudative otitis media, with its characteristic tendency to progressive deafness, has for its principal cause and continuous exciting factor some abnormality in the nose, pharynx or naso-pharynx—such as hypertrophied turbinates, deflected septum, hypertrophied or submerged diseased tonsils, or adenoids—is an accepted fact, probably settled beyond dispute. The relationship between the naso-pharyngeal condition and the commencing or progressing middle ear disease seems to have been thoroughly established and requires no special argument at this time. It is also an accepted fact that the early correction of such abnormalities is good prophylactic medicine, in that it tends to prevent the occurrence of affections of the middle ear. Furthermore, it seems to be the general belief that even after an acute exudative otitis media is established the ear can be restored to a normal condition and safeguarded for the future by prompt and proper treatment of the exciting factors in the nose or throat.

Assuming all this to be true, the possibility of curing or relieving an exudative otitis media that has reached the chronic stage, by removal of the naso-pharyngeal trouble, is not the subject of such universal agreement. As a matter of fact, there exists an attitude of skepticism in regard to any and all treatment of chronic exudative otitis media, on the part of the profession as well as of the public. There is abroad a false notion that this diagnosis always carries with it a hopeless prognosis as regards the auditory function and that the unfortunate patient is necessarily condemned to ultimate deafness, the rate of progress downward being more or less rapid according to circumstances. We must admit that there are many persons suffering with this affection for whom we can do little or nothing either in the way of curing the disease or of preventing its steady advance, but I am sure there are many more to whom the optimistic, skilled and patient attendant can render most helpful service. It is, however, not within the province of this paper to discuss the various forms of treatment that may be useful under the different conditions observed nor even to offer a classification of these variations. The single topic for present considera-

[1] Presented at the meeting of the American Otological Society, at Washington, May 7, 1913.

tion might be embraced in the question: What effect upon the ear can one logically expect from naso-pharyngeal surgery when the chronic exudative otitis media is believed to have had its origin in, or to be still excited by, abnormal conditions in the nose and throat?

I was led to ask myself this question several years ago for the following reasons: In the first place, I had found that some observers were doubtful of securing beneficial results to the ear from these operations and their doubts were based upon practical experience rather than disbelief in the theories upon which the treatment rested; for instance, cases which had presented every evidence of relationship between the aural and naso-pharyngeal affection had not been improved nor relieved, in so far as the ears were concerned, by the operation performed. As I shall attempt to show later, I think that many of these failures can be explained and that the doubts, though justified, were misplaced. Secondly, I desired to determine for myself a proper line of conduct toward these patients. Granting the existence of some naso-pharyngeal abnormality in association with a chronic otitis showing advancing deafness, what right had I to advise an operation within the nose or throat, when possibly these organs were not directly suffering, and what hope could I honestly and conscientiously hold out to the patient that such an operation would benefit his aural condition?

With a view to arriving at a definite answer to these questions, I have during the past few years carefully studied a series of such cases and it is to some conclusions drawn from these observations that I particularly wish to ask your attention. The small series of 34 cases upon which I shall report is taken entirely from my private practice; I have not attempted to study the records of those hospital and dispensary cases that were treated during the same period of time, because it is so difficult to follow up such cases in order to observe results and to keep the records accurate. In character the cases here under discussion are limited strictly to simple, chronic, exudative (catarrhal) otitis media associated with and believed to be dependent upon some naso-pharyngeal abnormality. No case is included which presented other complications, that is, such as involvement of the auditory nerve, otosclerosis, or the history of hereditary deafness.

A comparison of the conditions before and after treatment must unfortunately depend upon subjective tests and it is quite difficult to establish a test which shall be reasonably accurate and reliable and not subject to variations due to the personal equation of either the examined or the examiner. In every case the routine hearing tests were made, but most of these are of little value for comparison, with the object of answering the question propounded. The important facts to ascertain were whether or not the hearing was improved, remained stationary or had become worse immediately after the operation (meaning within two weeks), and, what the relative condition of hearing would be at a considerably later period. In looking over my records it still appears to me that the one and only test that could be utilized is one that I early came to look upon as the most practical and which might be called a self-controlled tuning-fork test. This fork, devised by Dr. Clarence J. Blake, and manufactured at the Lawrence Scientific School of Harvard University, is of the middle register ($C^2 = 512$ v. s.). It is set in action by drawing the prongs between the thumb and forefinger of one hand so that the tips are brought together by this pressure and spring apart of their own volition as they escape from pressure. The particular fork which I have used, and which has been repeatedly tested, can be heard by the normal ear for exactly 20 seconds when held at a distance of one inch from the meatus. It seems to me that this method is not open to the objection that applies to other means of setting a tuning fork in motion, such as striking it upon some object or with some form of hammer. No matter how much pressure is exerted the prongs can only be brought into contact and no matter how quickly released they can only spring apart; it is therefore scarcely, if at all, subject to any control upon the part of the examiner.

Perhaps it should be mentioned, too, if merely as a matter of acknowledgment, that what might be called a theoretical improvement in hearing is not necessarily one of practical value. For instance, ability to hear a moderately high-pitched tuning fork for a few seconds longer after treatment may not mean any greater ability to hear conversation. I used the test only as being the most reliable practical test of scientific value and believe that it fully serves the purpose here of indicating the direction of progress of the aural disease.

The accompanying table sets forth the age of the patient; the abnormal condition observed in the nose, pharynx or naso-pharynx; the duration of time in which the deafness had been increasing; the state of hearing by air conduction for the above named fork, expressed in fractions, the denominator representing the time that the fork should be heard by the normal ear and the numerator showing the time that it was actually heard; the operation performed; the immediate effect upon the hearing, according to the same test made within two weeks of the date of operation; and the condition of hearing, according to the same test, at the latest period thereafter that the patient was seen—which varied from six months to five years. The complaint in every case was increasing deafness and the period of time during which this had been observed varied from six months to fifteen years. Curiously enough, this longest-existing trouble (case No. 25) was one of those showing most marked improvement as the result of an operation.

Examination of this chart will show that in 32 cases there was immediate improvement of hearing to some degree; that in two cases there was no apparent change; that in none was there any immediate loss of hearing. A study of the later observations will show that of these 32 cases 26 remained improved, 4 showed additional improvement, and only 2 lapsed back from the first improvement to the previous state of hearing.

From a consideration of these cases I feel fully justified in answering my question with the following statement: Correction of the naso-pharyngeal abnormalities referred to—

hypertrophied turbinates, deflected septa, hypertrophied or submerged diseased tonsils and adenoids—in uncomplicated cases of chronic exudative otitis media will almost certainly check the advance of the aural disease, arrest progress of the deafness, and, in some instances, result in improvement of the hearing. It is impossible to predict in any given case that much improvement of hearing will follow and I am, in consequence, unwilling to hold out to any of these patients the hope of reclaiming any part of the lost hearing power. I usually tell them now that there is a reasonable certainty that further deterioration can be prevented; that there is a possibility, but not a strong probability, of reclaiming some part of what has been lost; and I usually find they are quite satisfied with the assurance that the disease can be arrested.

gist's point of view, the removal of these abnormalities must be accomplished in a manner thorough and complete, without injury to neighboring normal structures and with the object of restoring the parts to a normal anatomical and physiological status. Now of what avail is a nasal operation that results in an adhesion between the septum and the lateral wall? It would have been better to leave that turbinate or spur alone, for the nasal condition has not been improved, and, most certainly, no good effect upon the ear could be expected. An operation upon the tonsils which results in ablation of the faucial pillars (containing the palato-glossus and the palato-pharyngeus muscles) has, of course, disposed of the tonsils, but it can scarcely be expected to improve the function of the tubal muscles.

No.	Age, years.	Naso-paaryngeal abnormality.	Duration of increasing deafness.	Hearing for fork: C^2 (512 v. s.)	Operation.	Immediate hearing result.	Permanent hearing result.
1	39	Large adenoid, obstructing the tubal orifices.	Several years.	R. 10/20, L. 5/20.	Adenoidectomy.	R. 13/20, L. 19/20.	R. 17/20, L. 12/20, 2 yrs. later.
2	32	Hypertrophied rt. inf. turbinate; fibrous bands in Rosenmüller fossa.	2 years.	R. 8/20, L. 8/20.	Turbinectomy and removal of bands.	R. 10/20, L. 10/20.	Same, 6 mos. later.
3	24	Fibrous bands across left fossa of Rosenmüller.	6 months.	R. 20/20, L. 10/20.	Removal of bands.	R. 20/20, L. 15/20.	Same, 3 yrs. later.
4	35	Diseased submerged tonsils.	1 year.	R. 12/20, L. 7/20.	Tonsillectomy.	R. 15/20, L. 10/20.	Same, 6 mos. later.
5	14	Hypertrophied tonsils and adenoid.	1 year.	R. 20/20, L. 8/20.	Tonsillectomy and adenoidectomy.	R. 20/20, L. 16/20.	R. 20/20, L. 20/20, 2 yrs. later.
6	14	Hypertrophied tonsils and adenoid.	1 year.	R. 15/20, L. 10/20.	Tonsillectomy and adenoidectomy.	No change.	.....
7	17	Submerged tonsils and scar tissue.	Several years.	R. 5/20, L. 5/20.	Removal of tonsils and scar tissue.	R. 10/20, L. 8/20.	Same, 1 yr. later.
8	24	Deflected septum.	3 years.	R. 7/20, L. 1/20.	Submucous resection.	R. 10/20, L. 5/20.	Same, 1 yr. later.
9	18	Hypertrophied turbinates.	8 months.	R. 15/20, L. 15/20.	Turbinectomy.	R. 20/20, L. 20/20.	Same, 6 mos. later.
10	19	Hypertrophied rt. inf. turbinate.	2 years.	R. 10/20, L. 15/20.	R. infer. turbinectomy.	R. 14/20, L. 17/20.	R. 17/20, L. 20/20, 6 mos. later.
11	38	Deflected septum.	6 months.	R. 15/20, L. 12/20.	Submucous resection.	R. 19/20, L. 19/20.	Same, 1 yr. later.
12	24	Adenoid tissue about tubes.	5 years.	R. 7/20, L. 7/20.	Adenoidectomy.	R. 10/20, L. 10/20.	" 6 mos. "
13	21	Intumescent rt. inf. turbinate. Hypertrophied lt. middle turbinate.	3 years.	R. 20/20, L. 5/20.	Middle turbinectomy.	R. 20/20, L. 9/20.	" 5 yrs. "
14	33	Hypertrophied middle turbinates.	Several years.	R. 12/20, L. 3/20.	Turbinectomy.	R. 15/20, L. 8/20.	" 2 yrs. "
15	18	Hypertrophied tonsils.	2 years.	R. 12/20, L. 10/20.	Tonsillectomy.	R. 14/20, L. 15/20.	" 7 mos. "
16	26	Hypertrophied inf. turbs. and adenoid.	8 years.	R. 0/20, L. 12/20.	Inf. turbinectomy and adenoidectomy.	No change.	.....
17	32	Tonsil masses, previously burned.	3 years.	R. 17/20, L. 5/20.	Tonsillectomy.	R. 17/20, L. 9/20.	" 1 yr. "
18	31	Hypertrophied tonsils.	1 year.	R. 15/20, L. 20/20.	Tonsillectomy.	R. 20/20, L. 20/20.	" 1 yr. "
19	29	Submerged tonsils.	1 year.	R. 17/20, L. 10/20.	Tonsillectomy.	R. 20/20, L. 13/20.	" 6 mos. "
20	18	Hypertrophied tonsils and adenoid.	4 years.	R. 20/20, L. 8/20.	Tonsillectomy and adenoidectomy.	R. 20/20, L. 15/20.	" 1 yr. "
21	25	Adenoid.	7 years.	R. 18/20, L. 12/20.	Adenoidectomy.	R. 18/20, L. 18/20.	" 6 mos. "
22	16	Hypertrophied tonsils and adenoid.	12 years.	R. 5/20, L. 7/20.	Tonsillectomy and adenoidectomy.	R. 15/20, L. 16/20.	" 2 yrs. "
23	27	Diseased submerged tonsils.	Several years.	R. 8/20, L. 10/20.	Tonsillectomy.	R. 13/20, L. 15/20.	" 6 mos. "
24	18	Hypertrophied turbinates.	Several years.	R. 10/20, L. 6/20.	Infer. turbinectomy.	R. 15/20, L. 10/20.	" 6 mos. "
25	26	Hypertrophied middle turbinates.	15 years.	R. 6/20, L. 6/20.	Middle turbinectomy.	R. 18/20, L. 15/20.	" 6 mos. "
26	32	Submerged right tonsil and hypertrophied rt. inf. turbinate.	4 years.	R. 10/20, L. 12/20.	Tonsillectomy and turbinectomy.	R. 20/20, L. 20/20.	" 3 yrs. "
27	39	Intumescent inf. turbinates.	Several years.	R. 15/20, L. 10/20.	Cauterization of infer. turbinates.	R. 17/20, L. 17/20.	" 6 mos. "
28	33	Degenerate submerged tonsils.	3 years.	R. 10/20, L. 7/20.	Tonsillectomy.	R. 19/20, L. 13/20.	" 1 yr. "
29	26	Hypertrophied turbinates.	7 years.	R. 5/20, L. 5/20.	Cauterization of turbinates.	R. 10/20, L. 10/20.	" 1 yr. "
30	24	Submerged tonsils.	5 years.	R. 8/20, L. 15/20.	Tonsillectomy.	R. 15/20, L. 15/20.	" 6 mos. "
31	19	Hypertrophied tonsils and adenoid.	2 years.	R. 15/20, L. 10/20.	Tonsillectomy and adenoidectomy.	R. 18/20, L. 15/20.	" 6 mos. "
32	16	Hypertrophied turbinates.	2 years.	R. 10/20, L. 10/20.	Turbinectomy.	R. 15/20, L. 18/20.	" 6 mos. "
33	28	Hypertrophied tonsils.	13 years.	R. 15/20, L. 7/20.	Tonsillectomy.	R. 18/20, L. 10/20.	R. 15/20, L. 10/20, 2 yrs. later.
34	29	Diseased submerged tonsils.	10 years.	R. 5/20, L. 10/20.	Tonsillectomy.	R. 8/20, L. 7/20.	R. 5/20, L. 7/20, 2 yrs. later.

Now, I should like to revert to a consideration of that part of my first proposition which relates to the reason why so many failures and disappointments have followed naso-pharyngeal operations in chronic otitis media. I am convinced that the explanation lies in incomplete or improperly performed surgical procedures. Our conclusion that there is a definite connection between the naso-pharyngeal lesion, as a predisposing or active factor, and the slowly progressive chronic middle ear affection has for its foundation the belief that these abnormalities in the upper respiratory tract interfere with the normal physiological function of the tympano-pharyngeal tube. It matters not whether the effect upon the ear is produced by deflection of the air currents from their natural course through the nares, from mechanical obstruction of the mouth of the tube, from vaso-motor disturbances resulting from chronic inflammation, or from impairment of motion in the musculature of the soft palate and tubes; from the otolo-

During the time that I have been collecting the material embraced in this paper I have also had the opportunity of seeing some other cases that served to throw light upon these points. A young lady whom I had advised to submit to a tonsillectomy reported to me a year later that, in consequence of some tonsil surgery that she had witnessed while serving as a nurse at one of our general hospitals, she had so feared the operation recommended that she had preferred "to have the tonsils burned out by electricity." She had been subjected to nine cauterizations with the result that there was a mass of tonsillar and scar tissue to which the anterior and posterior faucial pillars were completely adherent. Not very long ago another patient returned to tell me that she had taken my advice and had her tonsils removed. That much was true, but it was not the whole truth; incidentally, the faucial pillars, on both sides, had been taken away, the operator making a clean sweep. It has even been seriously pro-

posed recently, by a surgeon in one of our large hospitals, that hemorrhage after tonsillectomy could be prevented (not controlled, mind you, but prevented) by suturing the anterior and posterior pillars together over the fossa as soon as the tonsil is removed. Can you think of anything less likely to benefit the middle ear? I can scarcely conceive of any circumstances requiring such suturing of these pillars; it certainly is not necessary either to prevent or control hemorrhage.

If such surgical work as this is performed upon patients suffering with chronic exudative otitis media it is not surprising that the aural disease is not arrested or benefited. Almost, if not quite, as bad as the effect upon the individual victim of such surgery is the fact that such results seriously discredit the work of competent surgeons; the otologist who has not received the right kind of assistance becomes discouraged and discards the only means of helping these patients, while the unfortunate victim goes out to decry all specialists. It goes without saying that I am not criticising any of that large body of our competent confrères working in this field, but every one of us knows that in every city and large town in this country numerous bungling operations of this sort are being performed daily by men without proper surgical training or knowledge of the specialty of rhino-laryngology. We are too frequently seeing or hearing of evil effects from operations in the nose or throat. For instance, of nasal operations that were frightfully painful; of tonsil or adenoid operations attended by profuse or even dangerous hemorrhage; or of some such injurious results as I have previously referred to. Now, any operation within the nose can be rendered absolutely painless if the cocaine be properly employed; and that does not mean using a large quantity. There is no reason whatsoever for the loss of more than a few drops of blood, a dram at the most, in a properly-performed tonsillectomy. Adenoidectomy is necessarily accompanied by some loss of blood, but even in this operation there need be nothing worthy the name of hemorrhage if a gauze tampon be applied and held in position for a short time immediately after removal of the adenoid. In regard to the tonsillar hemorrhages reported, I am reminded of a phrase I once heard Prof. Halsted use in the course of a lecture, which I cannot quote verbatim, but which was to the effect that hemorrhage in the course of an operation is the sole means the unconscious patient has to rebuke the incompetent or unskillful surgeon.

In conclusion, I desire to set forth emphatically my belief that simple exudative otitis media which is due to abnormal or diseased conditions in the nose or throat can be arrested in its progress by removal of these exciting conditions; that in such cases the progressive deafness can be stopped and further loss of hearing prevented; that in some few cases the hearing power may be materially improved; and that success of this kind depends, however, upon the proper performance of naso-pharyngeal operations so that there shall be complete and thorough eradication of the abnormality without injury to neighboring normal structures.

NOTES ON NEW BOOKS.

Disease in Milk. The Remedy Pasteurization. (*New York: 1913.*)

Mrs. Lina Gutherz Strauss says in her Foreword: "The presentation to the public of this book has a definite purpose, and is animated by a single hope. In calling the attention of others to the life work of my husband I trust that beneficent spirits may be stimulated to go and do likewise and achieve greater things for humanity." We also hope this, but what greater thing for humanity can anyone do than Nathan Strauss did in preventing illness among babies by giving away clean milk during the summer months of many years to the poor of New York city and elsewhere. He saved lives just as much as any doctor ever does, and many more than a single physician ever can and his name should ever be revered and loved for the work he did. It is only the rich who can accomplish such splendid results and were all the rich to employ their wealth to similar noble ends there would not be so many attacks on them, nor would they be so abused.

This collection of papers by Mr. Strauss is a valuable document as demonstrating to communities and individuals what can be done to help to keep babies well during the hot summer months—the cost is but small and the work simple, and it is to be earnestly hoped that others will forward this life-saving work.

The Operating Room and the Patient. By Russell S. Fowler, M. D. Third Edition Rewritten and Enlarged. Illustrated. $3.50. (*Philadelphia and London: W. B. Saunders Company, 1913.*)

This is naturally a popular work with a certain body of surgeons and students. It is serviceable for those who have not received a thorough surgical training for it goes into much detail of points which are essential to the good conduct of a surgical case, and which every man who expects to perform any operations should have at his fingers' ends before he undertakes work of this nature. It has a good index, is freely illustrated—not always in the best taste, however—and covers the ground satisfactorily.

Epidemic Cerebrospinal Meningitis. By Abraham Sophian, M. D. Illustrated. $3.00. (*St. Louis: C. V. Mosby, 1913.*)

The author had a very exceptional opportunity to study an epidemic of this disease in Texas—especially in Dallas, during 1912; and this work is largely a result of his observations at that time. He describes at length the etiology and symptomatology, then the laboratory diagnosis of meningitis, and its complications, and in two more chapters the results of studies in blood-pressure in meningitis, and treatment. This book which is a comprehensive study of this disease will needs be consulted when other authors are compiling descriptions of it, but for the ordinary student simpler and briefer accounts will suffice. The author has a long bibliography of names, but nowhere is there any reference to where the papers of the writers referred to can be found.

An Introduction to the Study of Infection and Immunity. Including Chapters on Serum Therapy, Vaccine Therapy, Chemotherapy and Serum Diagnosis. For Students and Practitioners. By Charles E. Simon, M. D. $3.25. (*Philadelphia and New York: Lea & Febiger, 1912.*)

The work is intended to be "an introduction to the study of infection and immunity and of the application of immunological principles to diagnosis and treatment." The first eleven chapters are devoted to a discussion of the general principles of immunity. The way in which micro-organisms injure the body is considered:

and the reaction of the body to this injury with antibody formation. The various "types" of immunity are described and their mechanism explained so far as possible. Ehrlich's hypothesis is extensively discussed.

In the second portion of the book the more practical applications of the subject are taken up. The various methods of immunization applied to man, especially active immunization by the use of vaccines, are well summarized. Especial attention is given to therapy: including the use of vaccines, and of tuberculin: of antitoxin, and other immune serum: and of salvarsan in syphilis. The last chapter is devoted to a too brief sketch of the commoner diagnostic reactions. The Widal reaction and the Wassermann reaction are described in some detail. The tuberculin and leutin reactions are illustrated by several excellent colored plates. On the whole the book is well written and should be of real service, as an "introduction to immunity." It is not detailed enough to serve as a comprehensive laboratory manual.

Flatulence and Shock. By F. G. CROOKSHANK, M. D. London. $1. (*New York: Paul B. Hoeber, 1913.*)

This thin volume is made up of two lectures which have little connection one with the other. The concluding paragraph of the first and the longer is: "But in strictest confidence, I will tell you this: should any of you, from overwork, overmuch tea, overmuch tobacco, or what not, get a spell of neurotic flatulence, and eructations with air gulping, nothing will give you so much relief as a bottle of the very best crème de menthe, sipped slowly and steadily until you are better," which seems to us pernicious if not dangerous advice. The lecture on Shock is a somewhat popular presentation of the subject, and adds nothing to our knowledge. Any adequate reason for collecting these papers together is not clear.

Golden Rules of Diagnosis and Treatment of Diseases. By HENRY A. CABLES, M. D. Second Edition. Revised and Rewritten. (*St. Louis: C. V. Mosby Company, 1913.*)

The title of the book is pretentious for the diseases treated are only those of the stomach, intestines, liver, gall bladder, pancreas and peritoneum, kidneys and bladder, blood, ductless glands, vascular system, lungs and pleural, and infectious and constitutional diseases. It is "intended to furnish a quick means of ready reference for physicians" and herein lie the dangers of these golden rules, works which we believe do more harm than good. The information given in them may be correct, but no one can really benefit by their use.

Dreams and Myths. A Study in Race Psychology. By DR. KARL ABRAHAM, Berlin. Translated by WILLIAM A. WHITE, M. D. Journal of Nervous and Mental Diseases, Monograph Series, No. 15 (*New York, 1913.*)

In sagas and legends it is a well known fact that folk phantasy finds expression, and in this work an attempt is made to compare myths with the phenomena of individual psychology, especially with dreams. As Freud's psycho-analytic method gradually became elaborated, it was found that a searching investigation of the dream-state was essential for the full understanding of the personality of the individual. According to Freud there lies at the bottom of every dream a repressed wish in the unconscious, and the deepest roots of this wish lie in the childhood of the dreamer. It is very clearly shown, for instance, how the common dream of the death of a near relative can be traced back to an infantile wish, and how erroneous it is to assume that the feeling of the child for its parents, and brothers and sisters is from the first, one of love. The above points are further elaborated and explained in connection with the Oedipus saga.

Abraham takes the Prometheus saga as an example of a symbolic myth, and subjects it to the same method of interpretation as that of a dream analysis. He proves clearly and convincingly how the factors of condensation, displacement, secondary elaboration, and wish fulfillment which are almost invariably present in dreams are also present in the Prometheus saga, and concludes by making the following statement: "As Freud has shown for the Oedipus saga so I believe I have established for the Prometheus saga that it has not taken its origin from ethical, religious, or philosophical considerations, but from the sexual phantasies of mankind."

This book of Abraham's is an exceedingly interesting and stimulating one, and is well worthy of the most careful study by every student of psycho-pathology.

The translation is excellent.

Solidified Carbon-Dioxide. By RALPH BERNSTEIN, M. D. Illustrated. (*Hammond, Ind.: Frank S. Betz Co., 1912.*)

The author is somewhat enthusiastic on the use of solidified carbon-dioxide, as the following quotation from the preface will indicate: "That we have in solidified carbon-dioxide the remedial substance par excellence in the treatment of cutaneous neoplasms, both benign and malignant, cannot now be denied, and which, from clinical evidence, because of its superiority, will eventually take the place of the x-rays and the many inferior chemical substances in common usage."

The principle value of the little book lies in the detailed technic of the preparation and use of solidified carbon-dioxide. There is no doubt of the efficacy of this substance in the treatment of a number of skin lesions, but it hardly seems wise, as yet, to abandon for it all other well established and successful methods of treatment

J. S. D.

Clinical Laboratory Methods. A Manual of Technique and Morphology, designed for the use of Students and Practitioners of Medicine. By ROGER S. MORRIS, A. B., M. D. First Edition. (*New York and London: D. Appleton & Co., 1913.*)

Medical literature is at present abundantly supplied with books which deal, in a fairly exhaustive manner, with the various topics generally included under the title "Clinical Diagnosis." By their use physicians and students should become familiar with the fallacies, advantages and interpretations of the common and more unusual tests applied for diagnostic purposes. It is not, however, to be expected that anyone will burden his mind with the actual operative details of many of the tests themselves. Indeed, a great part of modern medical education consists in knowing where to find authoritative opinions and reliable methods when needed.

A ready reference library is admirably provided for the busy men who wisely take advantage of the aids which clinical laboratory methods afford to the sciences of diagnosis and treatment, in the book just written by Dr. Morris. As stated by the author, "the significance of the abnormal is not discussed"; the space is simply allotted for the statement of how to apply qualitative tests and quantitative methods of proven value. There has been, moreover, a careful omission of procedures which are in any way too exacting or time-consuming. In many instances several methods are given thus allowing one a free choice. The "sources of error" paragraphs, which follow most of the tests, are invaluable and should make faulty interpretations a negligible quantity. Wherever it has seemed necessary, footnotes give references to valuable original articles or exhaustive treatises. In this manner the subjects of urine, gastric juice, fæces, sputum, blood and puncture fluids have been admirably covered, yet in a book of convenient size, well printed and illustrated by 46 well-chosen cuts, and two colored plates, drawn by the author, depicting the various blood cells as stained by the Ehrlich and Romanowsky methods. The

latter is especially to be commended. Where methods involve calculations, as, for instance, the quantitative determination of urinary chlorides, examples are given which make the successive steps clearly understood.

The style of the book is pleasing and reflects both the author himself and his wide practical knowledge of the subjects treated. Errors are singularly few. Indeed, with the aim of the book in mind, it is hard to see how it could be improved upon. There is no other work like it and the reviewer would earnestly urge its purchase and constant use by those for whom it was preeminently written—practitioners of clinical medicine. S. R. M.

Müller's Serodiagnostic Methods. Authorized Translation from the Third German Edition, 1913. By Ross C. Whitman, B. A., M. D. (*Philadelphia and London: J. B. Lippincott Company.*)

This little volume of 143 pages has much to commend it. It is in no sense an exhaustive work, nor does it attempt to discuss the theories upon which many of the described methods are based. It assumes a knowledge on the part of the individual of the fundamental laws and concepts of immunity, and their general application to the wide field of serology. It likewise assumes at least some knowledge and practice in serological technique. "The chief emphasis has been laid on making the description of the various methods as exact as possible, and especially on giving a complete and detailed list of the reagents and apparatus required for each test."

Methods of injecting animals—bleeding them and the preservation of sera—are concisely given. The various diagnostic methods are in general treated under four headings: (a) The principle involved; (b) the field of application for the test; (c) the apparatus required; and (d) the technique of application. Discussions and interpretations of results have been for the most part omitted. Certain tests of doubtful value, such as the cobra venom, Much-Holzmann, and meiostagmin reactions have purposely been included, in the hope of stimulating further work on them and other lines of research which they suggest. Though the book should "lighten the labor of the beginner" or practiced worker in the field of serology, it should only be used in conjunction with others of a more critical and theoretical nature. The possession of such a book will, however, never be regretted. S. R. M.

Laboratory Methods. With Special Reference to the Needs of the General Practitioner. By Drs. B. G. R. Williams and E. G. C. Williams. Second edition. Illustrated. $2.50. (*C. V. Mosby Company, St. Louis, 1913.*)

The value of this work lies in the fact that it demonstrates that a general practitioner can do a lot of laboratory work at a slight cost and with simple appliances, and there are many practitioners living remote from cities who will find this book a most useful and clear guide in any investigation they may want to pursue. That a second edition of this work has been called for shows how wide awake many of our country doctors are, and how they try to keep up their studies under difficulties. We hope this new and improved edition will have a still larger circulation.

International Clinics. Vol. II. Twenty-third series. $2.00. (*Philadelphia and London: J. B. Lippincott Company, 1913.*)

The contents of this volume are of the same varied character as those of the preceding volumes; there is both entertainment and instruction to be drawn from these clinics, and one of their most important uses is in making known the various writers to the many readers. It is a valuable form of instruction—learning to know about men by their writings—and in these volumes one has the opportunity to measure the "bigness" of many contributors, and so learn what to read and what to leave unread.

Progressive Medicine. Vol. II. June, 1913. (*Philadelphia and New York: Lea & Febiger.*)

The review of hernia and surgery of the abdomen consume 186 pages of this volume, gynecology a little over 100, and diseases of the blood, thyroid gland, nutrition, the lymphatic system, and diathetic and metabolic diseases about 115, and ophthalmology not quite 30. These figures are merely noted to show the subjects which seem to receive the greatest attention in the general medical literature. The deduction may not be quite accurate, for those responsible for the different chapters may prepare reviews of very varying length; but there is no doubt that the relative importance of the various subjects dealt with in this volume is fairly represented here, and the readers will, in reading the reviews, get a just impression of the work being done in Europe and America in these lines of science.

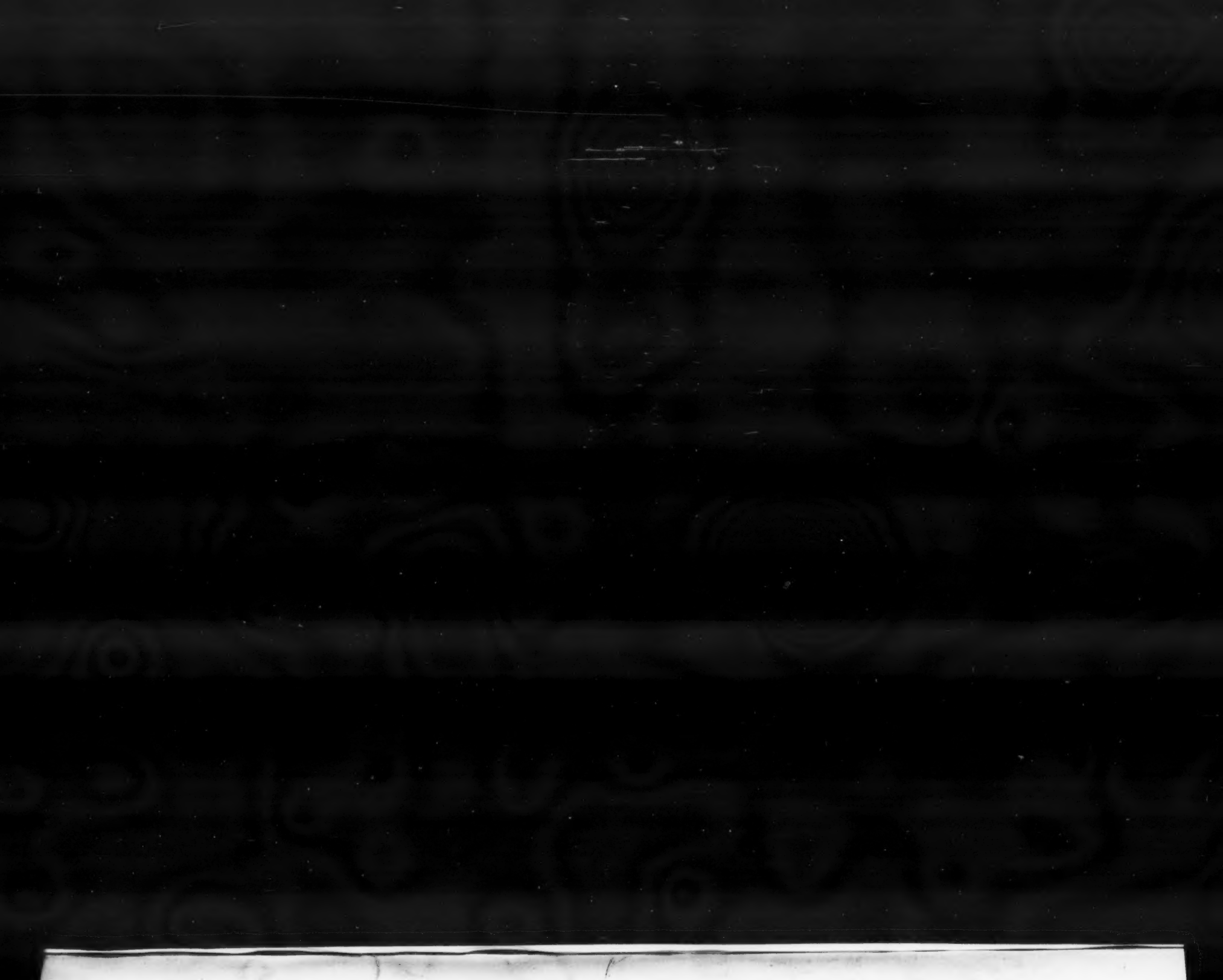
Hygiene and Sanitation. A Text-book for Nurses. By George M. Price, M. D. $1.50. (*Philadelphia and New York: Lea & Febiger, 1913.*)

The field of work for nurses has widened so greatly in the last few years that many books, besides those directly dealing with the care of the sick, are needed for their instruction, and this small volume will be welcome to a large body of women now engaged in various branches of social service work. The author's manual is simple and covers the subject satisfactorily; he discusses tersely the hygiene of dwelling houses, foods, schools, occupations, municipalities, etc., and has written a helpful introduction for broader study of these subjects for those who wish to make themselves proficient in any one of these subdivisions of hygiene.

Stammering and Cognate Defects of Speech. By C. S. Bluemel. $5.00. (*New York: G. C. Stechert and Company, 1913.*)

The author's theory of stammering, that it is due to transient auditory amnesia, has been evolved, in large part, he says, "as the result of introspective evidence; evidence as indispensable as it was uncoveted"; and to this theory he devotes the first volume of his work, the second being given over in large measure to a description of "contemporaneous systems of treating stammering: their possibilities and limitations." The second volume thus serves as an historical review of the subject, and contains in addition a glossary of words, the most of which any intelligent reader should understand without looking up, and a very long bibliography. Further evidence, possibly of an experimental nature, will have to be brought to substantiate the author's theory, and meantime psychologists will be interested in applying this idea to a study of their own cases.

Diseases of the Eye. By George E. de Schweinitz, M. D. Seventh edition, thoroughly revised. Illustrated. $5.00. (*Philadelphia and London: W. B. Saunders Company, 1913.*)

Dr. de Schweinitz's work requires no word of commendation from us. Its admirable qualities have long since been recognized by the medical profession, and its seventh edition is but a new proof of its excellence. The author's reputation is world-wide and his book has been for many years one of the standard treatises on diseases of the eye.

The Johns Hopkins Hospital Bulletins are issued monthly. They are printed by the LORD BALTIMORE PRESS, Baltimore. Subscriptions, $2.00 a year (foreign postage, 50 cents), may be addressed to the publishers, THE JOHNS HOPKINS PRESS, BALTIMORE; single copies will be sent by mail for twenty-five cents each. Single copies may also be procured from the BALTIMORE NEWS CO., Baltimore.